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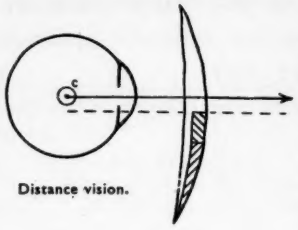
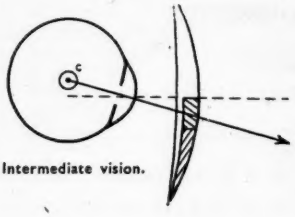
FUSED TRIFOCAL LENSES

Presbyopes with a reading addition of +1.50D or more, often experience difficulty in becoming accustomed to the sudden change of power between the two portions of bifocal lenses.

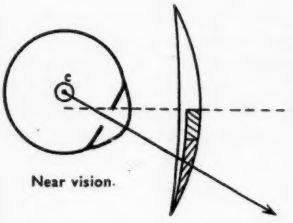
Trifocal lenses, which are made in fused form, present an intermediate portion whose power is exactly half-way between those of the distance and reading portions. This intermediate portion, as well as lessening the call on accommodation, markedly diminishes the "jump" experienced with the usual type of bifocal lens, due to lack of correspondence of the two centres; in this respect trifocal lenses are comparable with Hamblin's "No-jump" bifocals. The elimination by trifocal lenses of that intermediate zone in which an advanced presbyope is otherwise unable to focus his vision has led to their becoming known in America as "continuous vision lenses".



Distance vision.



Intermediate vision.



Near vision.

c = centre of rotation

Trifocals, often desirable, become invaluable to presbyopes in those occupations necessitating clear vision of that part of the foreground which is outside their reading distance. Wearers such as painters, who work largely at arm's length and those who must interview other people, as must most professional men, find these lenses of particular service.

The diagrams show the principles of fitting trifocals, a procedure requiring considerable care. Hamblin's, in over twenty years' experience of dispensing them, have been impressed by the readiness with which presbyopes, although unsatisfied by bifocals, will accept trifocal lenses.

In order to enable more surgeons and patients to become familiar with their advantages, Hamblin's will willingly replace with bifocals any trifocals fitted by them and not found satisfactory. No charge will be made for this service, but the patient should have worn the glasses for a trial period of six weeks and should return them in good condition within a further two weeks if he wishes to have them replaced.

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Brit. J. Ophthal. (1953) **37**, 65.

COMMUNICATIONS

RETINAL PHOTOGRAPHY IN COLOUR

BY

PETER HANSELL AND E. J. G. BEESON

Medical Illustration Dept., Institute of Ophthalmology, London, and the Research Laboratory, British Thomson-Houston Co., Ltd.

HISTORICAL.—Monochrome photography of the human retina has been practised increasingly since the early pioneer work on this subject in the latter half of the 19th century. The instrument in most common use to-day is the Zeiss-Nordenson retinal camera, which first appeared in 1915. Several modifications of the original instrument have since appeared, and over 10 years ago it was reported that about 350 of these cameras had been distributed by the manufacturers (Koch, 1941). The early models employed a carbon arc light source, and later an incandescent lamp was used. The general appearance of the apparatus is shown in Fig. 1.

Colour photography of the ocular fundus has been developed relatively recently; early results on Dufaycolor and Agfacolor were hardly satisfactory, but Kodachrome began to be used successfully about 1935.

Many collections of Kodachrome transparencies have by now been made, and the Zeiss-Nordenson carbon-arc model has been favoured for this purpose. It is also interesting to note that, after much research, the Bausch and Lomb Co. have reverted to the use of a carbon-arc in their new retinal camera (*Med. biol. Illus.*, 1952, **2**, 58).

Various workers (Bedell, 1940; Koch, 1941) have reported that exposure times of $\frac{1}{2}$–$1\frac{1}{2}$ sec. are necessary to obtain results with this type of subject and equipment. With exposures such as these, there is a considerable risk of records being marred by movement of the subject, and the unstable nature of an open carbon arc makes serial recording unpredictable. These diffi-

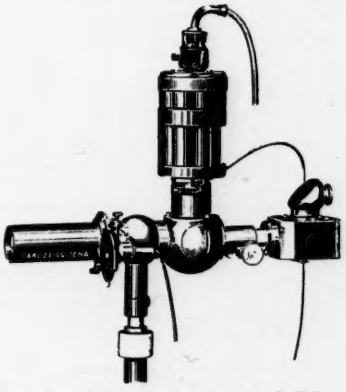


FIG. 1.—General appearance of Zeiss-Nordenson retinal camera.

culties chiefly encouraged us to look for an improved light source and determined the final choice.

Development of the FA5 Xenon Lamp

The present work has been concerned with the development of a new light source to be used with a Zeiss-Nordenson camera for colour photography of the retina. The basic requirements were taken to be:

(*i*) The illumination should be sufficiently constant to allow alignment and focusing of the optical system and visual examination of the retina without discomfort to the patient.

(*ii*) The light-source should be stable, constant, and of a spectral emission suited to colour-film sensitivity.

(*iii*) The illumination should be greatly increased for the actual moment of photographic exposure. To minimize discomfort and involuntary movement and blinking on the part of the patient $\frac{1}{25}$ sec. should be the maximum permissible exposure.

A dimensioned drawing of an experimental lamp (BTH, FA5) is given in Fig. 2. The first requirement can be met by operating this lamp as a continuous arc at a current of 10 amps with a potential of 15 volts.

The second requirement is achieved by filling the glass envelope of the lamp with pure xenon which gives a spectral emission approximating daylight.

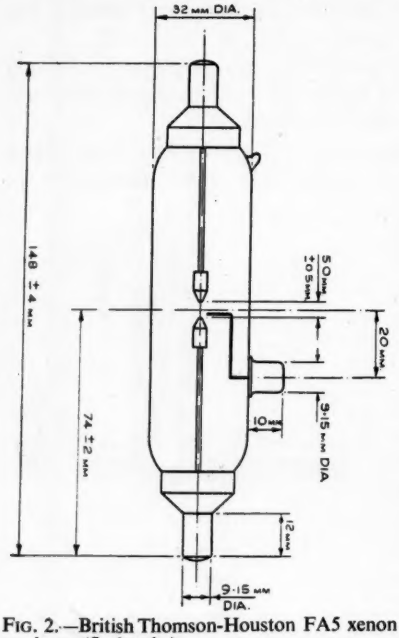


Fig. 2.—British Thomson-Houston FA5 xenon arc lamp (flash tube).

The first line of approach to the third problem, that of providing intense illumination for exposure, was to run the lamp as a continuous arc for focusing, and then to switch off and pass a condenser charge through the tube in the same manner as an "electronic flash". Tests revealed several disadvantages, the first of which was the length of time required to allow the electrodes to cool sufficiently to prevent auto-triggering of the condenser flash, and the noise produced by the sudden discharge was another undesirable feature. The main reason for abandoning this method, however, was that, with increasing energy, the light source increased in *size* rather than *intrinsic brightness*. As there

are two limiting apertures in the system—one in the camera and the other the pupil of the eye—nothing could be gained from a larger source; adequate results were obtained on fast monochromatic film, but the effective light was insufficient to expose colour film.

Another possibility was that of over-running or pulsing the lamp at a high current for an instant during its normal running as a 150w continuous arc. Tests made with a compact source mercury discharge lamp (Type ME) and a slow monochromatic film showed that the xenon lamp would require to be pulsed at some 5,000w to achieve results on colour film at an exposure of $\frac{1}{25}$ second. With the equipment to be described, it is indeed possible to overexpose Kodachrome film at this speed.

A control unit for this pulse operation has now been developed. A detailed specification is outside the scope of this paper, but full technical data are available and a simplified circuit and description are given in Fig. 3.

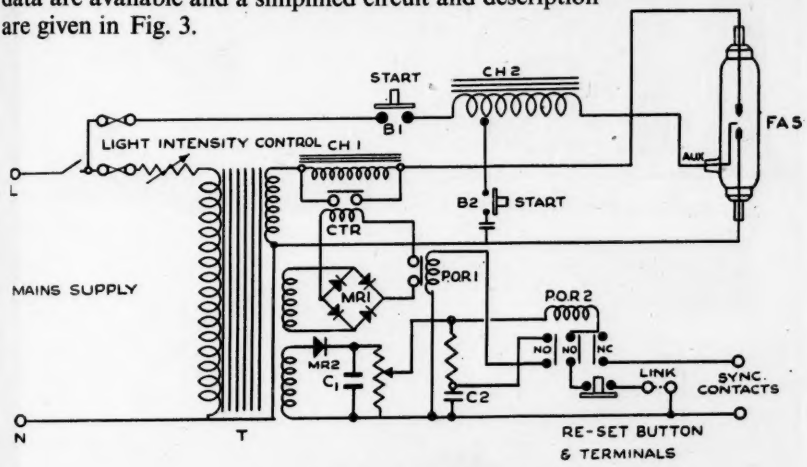


FIG. 3.—Xenon lamp pulse circuit.

The circuit design is for normal 200/250v 50-cycle AC operation providing current to the FA5 lamp at 40 volts. On closing the main switch the two main lamp electrodes are made alive. As the gas pressure in the lamp is high at room temperature, it is necessary to provide a surge of voltage from transformer CH.2 to the auxiliary electrode on the lamp by closing push button B_1 and intermittently opening and closing the start button B_2. The intermittent operation of button B_2 causes a peaking 50-cycle AC voltage to initiate the auxiliary arc. Once this arc discharge has been established by further intermittent closing and opening of B_2, B_1 still being held closed, the main arc gap breaks down, and once the two main electrodes have reached a temperature high enough, the auxiliary arc is extinguished by releasing button B_1. The lamp is now running at a steady power of approx. 150w.

To pulse the lamp, synchronizing contacts are provided which, when shorted together, close P.O. relay 2. The contacts on this relay in turn close and complete a further circuit to cause the charged condenser C2 to be discharged through P.O. relay 1. The closing of relay POR. 1 in turn closes a high speed contact CTR which momentarily allows a heavy current to flow through the lamp. Normally the current in the lamp is limited by the series choke CH.1. The value of the current in the lamp is controlled by the variable resistance in the primary circuit of the main transformer, and the duration of the flash by the energy stored in the condenser C.2. and discharging this through P.O. relay 1. The timing of this circuit is pre-set to give a flash of light with a duration of $\frac{1}{250}$ — $\frac{1}{25}$ sec. After each flash the circuit requires to be reset, and as well as the toggle switch provided for this purpose a link is also supplied so that automatic resetting and tripping of the circuit can be arranged independently of any manual operation.

The voltage and current necessary to trip the circuit are of such a value that a micro-relay or normal camera contacts are adequate to trip the flashing of the lamp.

Use of the FA5 Xenon Lamp with the Zeiss-Nordenson Camera

The lamp is of such a size that it may be mounted vertically on the Zeiss-Nordenson camera in the position normally occupied by the carbon-arc housing (Figs 4 and 5). The electrodes can be positioned in relation to the

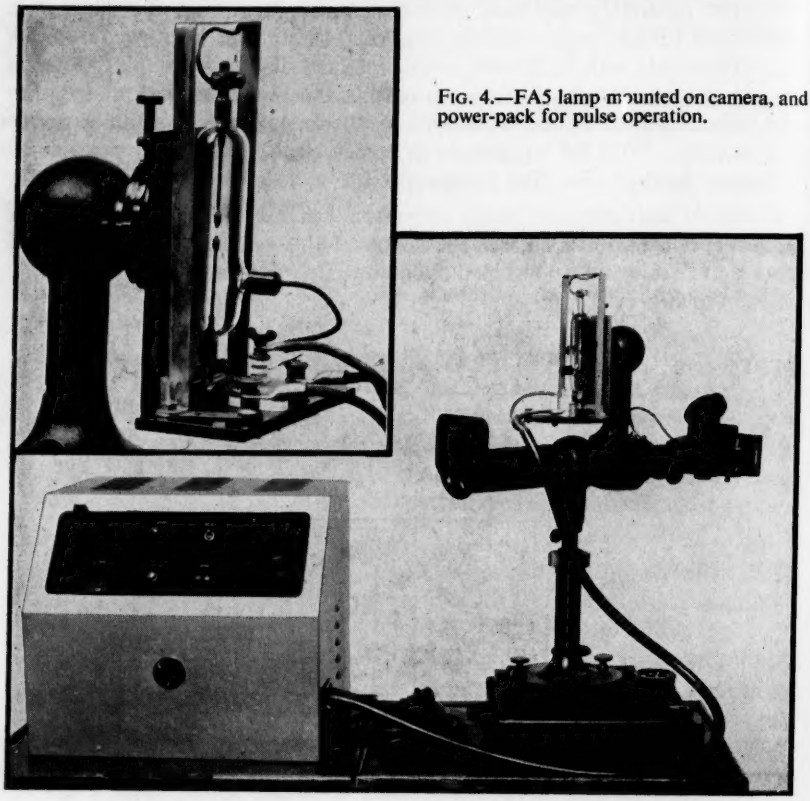


Fig. 4.—FA5 lamp mounted on camera, and power-pack for pulse operation.

first condenser, and thereafter the vertical and horizontal slides provided on the instrument can be used for centring the arc.

The level of illumination emitted when the lamp is burning normally is lower than that of the original carbon arc, and therefore the neutral density filter in

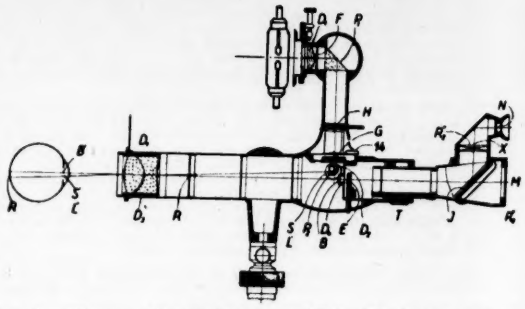
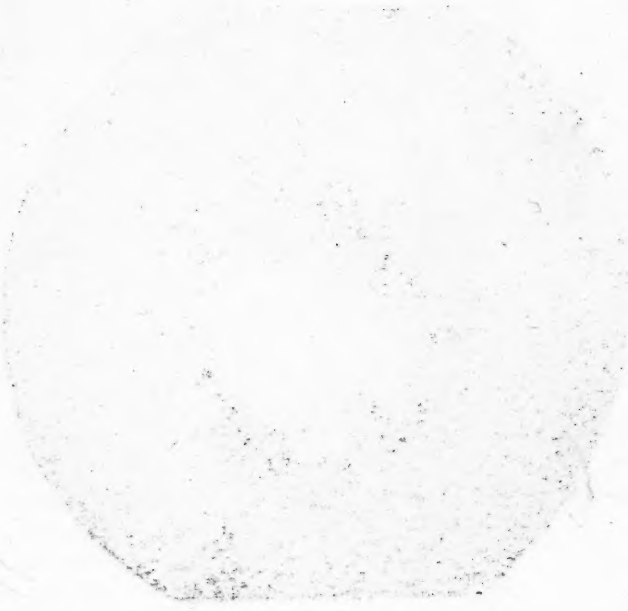


Fig. 5.—Diagram of optical system of Zeiss-Nordenson camera, showing position of FA5 lamp.

FIG. 6.—Kodachrome Bantam frames obtained at $\frac{1}{25}$ sec. with FA5 lamp.
(*a*) Congenital anomaly of left optic disc.
(*b*) Toxoplasmosis of right eye.



the shutter must be replaced by a lighter one to provide enough transmission for visual focusing and examination of the retina.

The pulsed high-intensity illumination is limited to $\frac{1}{25}$ sec. by the control unit, and it is therefore necessary to synchronize this with the shutter opening. In practice it has been found convenient to trigger the pulse by mechanical contacts activated by the shutter mechanism itself. To obviate the necessity for fine control and delay mechanisms, it is advisable to fit the $\frac{1}{25}$ sec. pulse into a shutter opening of $\frac{1}{10}$ sec.

Finally, the camera back has been modified to accept Bantam roll film, for Kodachrome film is available in this size in eight-exposure lengths; furthermore, the picture size is slightly larger than that obtained on 35 mm. film. A similar modification has been described by Markham (1951). Fig. 6 is a reproduction of two Kodachrome Bantam frames made with the above equipment.

OTHER APPLICATIONS.—The FA5 lamp has characteristics which make it suitable for other uses. Where constant adjustment and focusing of an optical system are required, the steady source of light together with the ability to produce a flash at a desired moment, would meet many needs in slit-lamp photography. In photomicrography and time-lapse photography of living matter the heating problem normally encountered is considerably reduced by the very brief duration of the pulsed flash. The fact that this lamp can also be operated by condenser discharge adds to the range of its possible uses. It has already been used as a compact stroboscopic source with a repetition frequency exceeding 160 flashes per second.

SUMMARY

The application of a new compact xenon arc lamp (FA5) to retinal photography in colour is described. The circuit required for pulse operation of the lamp is given and some modifications of the Zeiss-Nordenson retinal camera are mentioned.

By these means standard and comparable records of the fundus oculi may be obtained on Kodachrome colour film at exposures of $\frac{1}{25}$ sec.

We should like to thank members of the staff of the Institute of Ophthalmology and of the research laboratory of the British Thomson-Houston Company for helpful advice and facilities for experiment.

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STELLATE GANGLION BLOCK IN GLAUCOMA*

BY

S. J. H. MILLER

From the Glaucoma Clinic, Institute of Ophthalmology, London
Director of Research: Sir Stewart Duke-Elder

THE influence of emotional tone in congestive glaucoma suggests that the sympathetic nervous system may be the mediator whereby attacks of raised intra-ocular pressure are precipitated. The idea is not a new one and has suggested itself to many (Lagrange, 1922). Jonnesco (1899) made wide claims for the effectivity of resection of the sympathetic in the neck in the management of glaucoma, but Linksz (1931) found that the intra-ocular pressure was more labile after cervical sympathectomy. Further research has not been devoted to the subject, but the recent discovery by Nickerson and Goodman (1945) of the sympatholytic drug, dibenamine, and of its hypotensive effect in glaucoma (Christiansen, Swan, and Gould, 1948) has led to a renewal of interest in the possible role of neurogenic factors in the aetiology of this disease.

This paper records the responses of thirty glaucomatous eyes to local block of the stellate ganglion with procaine. The anterior approach to the ganglion is fully described by Leriche and Fontaine (1934), Gilbert and Takats (1948), and Moll (1951). I am indebted to the late Mr. E. R. Garnett Passe for personally demonstrating his method to me (Passe, 1951).

Method

The patient lies in the supine position with the head turned to the opposite side through an angle of 45°. A pillow is placed under the scapula on the side of injection. A point is chosen 1 in. above the clavicle just internal to the external jugular vein, about 0.5 to 1 in. behind the medial border of the sternocleidomastoid muscle. A bleb is raised in the skin with procaine hydrochloride 1 per cent. solution. The needle is inserted through the bleb directed backwards, medially and horizontally, lateral to the great vessels. The transverse process of C7 is felt by the needle after it has penetrated about 2 in. The point of the needle is then made to travel along the upper border of the process until it strikes the body of this vertebra; the needle is then withdrawn slightly and, after it has been ascertained that the point is neither in a blood vessel nor in the spinal cord, 5 to 10 ml. procaine are slowly injected.

Criteria of an Effective Block.—A Horner's syndrome begins to appear on the side of the injection before the needle is withdrawn. Contraction of the pupil is the more sensitive index of a successful block, but narrowing of the palpebral fissure also becomes well marked. The two signs reach their maximum in 10 to 20 min., and gradually wear off during the ensuing hour. Flushing and warming of the skin with absence of sweating appear over the head and neck on the same side, and extend along the upper extremity to the hand. The vessels of the conjunctiva and the tympanic membrane are dilated and form an accurate indication of success or failure.

* Received for publication December 8, 1952.

Results

A study of the results of stellate ganglion block shows the following changes affecting the ocular tension and the behaviour of the aqueous veins.

(A) Pressure Changes

(1) IN SIMPLE GLAUCOMA.—There is an immediate rise in intra-ocular pressure, which lasts for approximately 10 mins, and is followed by a fall to the original pressure and somewhat below it (Fig. 1).

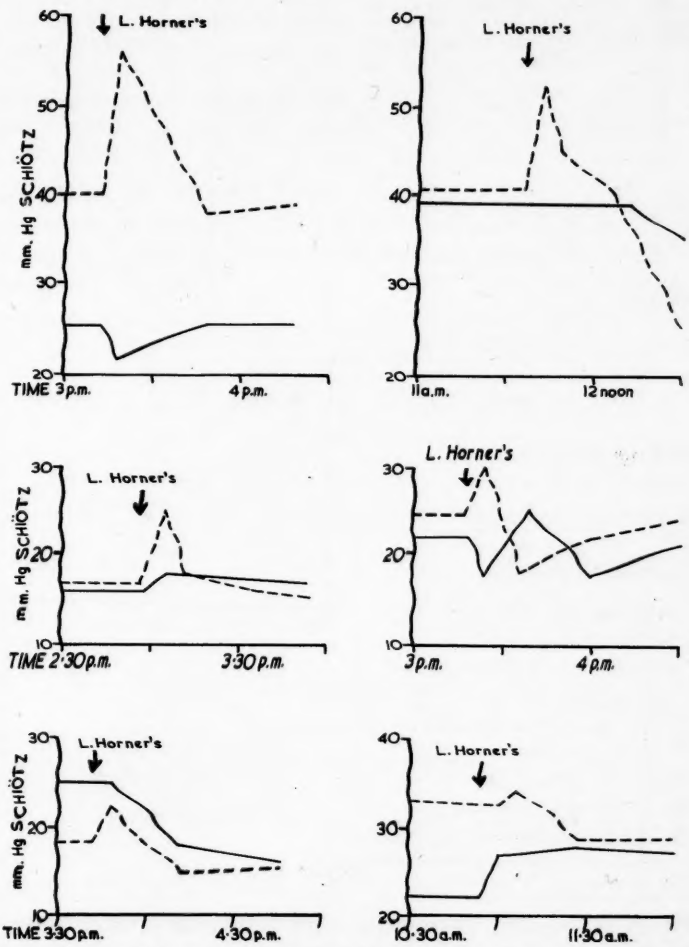

FIG. 1.—Intra-ocular pressure (mm. Hg Schiötz) in six cases of simple glaucoma charted before and after unilateral block of stellate ganglion.

(2) IN CONGESTIVE GLAUCOMA

(*a*) *With a structurally open angle.*—The intra-ocular pressure falls at once to levels below that found before injection (Fig. 2).

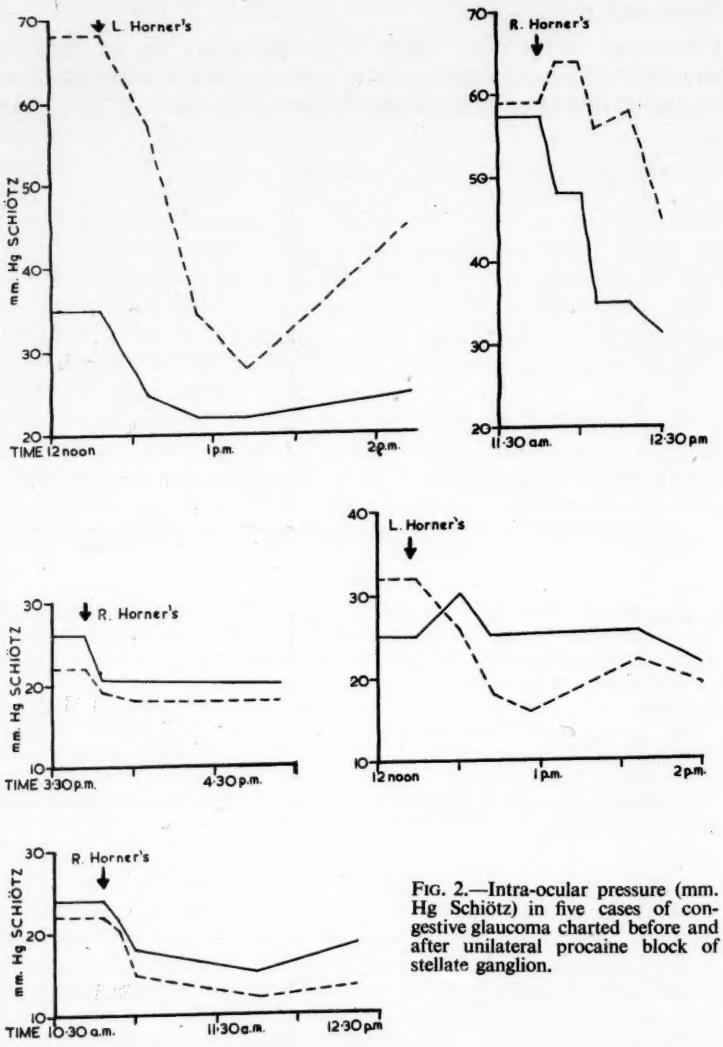

FIG. 2.—Intra-ocular pressure (mm. Hg Schiötz) in five cases of congestive glaucoma charted before and after unilateral procaine block of stellate ganglion.

(*b*) *With a partially closed angle.*—The intra-ocular pressure behaves as in simple glaucoma: an initial rise is followed by a fall. Fig. 3 (opposite) shows the curve of the intra-ocular pressure following stellate ganglion block in a

patient aged 31 years who had complained of attacks of halos, blurred vision, and ocular pain for 2 years. His fields of vision were full and his disks not cupped. Gonioscopy revealed persistent mesoderm in both chamber angles.

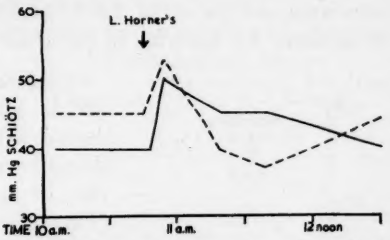

FIG. 3.—Intra-ocular pressure (mm. Hg Schiötz) in a case of congestive glaucoma with persistent mesoderm in the angle of the anterior chamber charted before and after unilateral procaine block of stellate ganglion.

(*c*) *With a completely closed angle.*—The intra-ocular pressure rises at once and there is no subsequent fall; in effect, an acute attack of glaucoma is precipitated. Fig. 4 depicts the rise in intra-ocular pressure in a patient who had long-standing congestive glaucoma with the formation of total peripheral anterior synechiae.

(B) BEHAVIOUR OF AQUEOUS VEINS

(1) IN SIMPLE GLAUCOMA.—The recipient laminated veins at first fill with blood and regain their laminated appearance when the intra-ocular pressure begins to fall.

(2) IN CONGESTIVE GLAUCOMA.—The aqueous veins remain clear throughout the period of observation if the angle is structurally open.

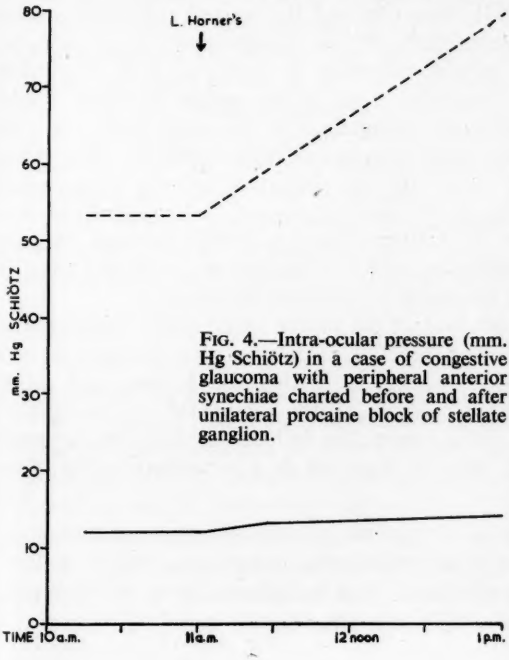

FIG. 4.—Intra-ocular pressure (mm. Hg Schiötz) in a case of congestive glaucoma with peripheral anterior synechiae charted before and after unilateral procaine block of stellate ganglion.

Analysis of Results

The results of novocaine block of the stellate ganglion may be discussed under four headings:

(1) *Pupillary Effect.*—The pupil contracts on the side of the injection even in the dark. In simple glaucoma, it is to be remembered that the size of the pupil has little effect on intra-ocular pressure, for dilatation has no influence on the height of the intra-ocular pressure provided the angle of the anterior chamber is broad and open. In congestive

glaucoma, on the other hand, pupillary constriction facilitates the outflow of aqueous by opening up the angle of the anterior chamber (Fig. 5).

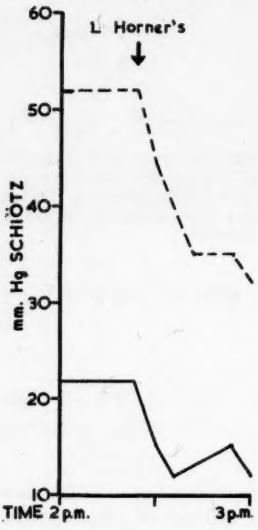

FIG. 5.—Intra-ocular pressure (mm. Hg Schiötz) in a case of congestive glaucoma charted before and after unilateral block of stellate ganglion carried out in the dark.

(2) *Dilatation of Intra-Ocular Capillaries.*—In simple glaucoma, dilatation of the intra-ocular capillary bed cannot be rapidly compensated by displacement of intra-ocular fluid because the rate of drainage of aqueous is below normal (Thomassen, 1946; Grant, 1951), so that a sudden and early rise of intra-ocular pressure occurs. In congestive glaucoma it seems probable that, so long as the angle is open, a dilatation of the intra-ocular capillary bed immediately displaces aqueous from the eye, and that the increased intra-ocular capillary volume is so rapidly and effectively compensated that the height of the intra-ocular pressure remains unaffected.

(3) *Dilatation of Veins.*—It is claimed that throughout the body generally the sympathetic system exerts a tonic influence on veins and that section of the sympathetic leads to their dilatation in man (Wright, 1952). In the eye, Wagener (1931) has watched the retinal veins dilate after interruption of the sympathetic nerve supply. It would therefore be expected that a sudden sympathetic block of the stellate ganglion would produce a relaxation of the veins and a fall in the lateral pressure of their contents. This effect would be reinforced as a result of the dilatation of the intra-ocular capillary bed which becomes a temporary reservoir. It is well known that in histamine poisoning the venous return is greatly reduced because the blood stagnates in the capillaries, and it is possible that a similar effect is produced in the exit veins of the eye after sympathetic block.

Thomassen (1945) has shown that, in the phasic variations of glaucoma, a fall in venous pressure precedes the fall in intra-ocular pressure in the descending phase. The exact mechanism linking the venous and intra-ocular pressures has yet to be elucidated. If the venous fall is causative, as suggested by Duke-Elder (1952), then the fall in intra-ocular pressure following sympathetic block may be regarded as a secondary result of its effect on venous pressure.

(4) *Formation of Intra-Ocular Fluid.*—It is probable that the formation of the intra-ocular fluid is equally affected by sympathetic block in both types of glaucoma, and that this factor does not contribute to the difference in the reactions of their intra-ocular pressures.

These factors may be summarized as follows:

Effects of Sympathetic Block	Effect on Intra-ocular Pressure	
	Congestive	Simple
Pupillary constriction	Fall facilitated	No effect
Dilatation of intra-ocular capillaries ...	No effect	Rise
Lowering of venous pressure	Fall	Fall

Discussion

In simple glaucoma, the events following stellate ganglion block are probably determined by a dilatation of the intra-ocular capillaries causing an increase in the volume of the intra-ocular capillary bed. A corresponding volumetric displacement of aqueous through the drainage channels is not immediately possible because of the reduced capacity for drainage characteristic of this disease (Thomassen, 1946; Grant, 1951) and the net effect is therefore a temporary rise in intra-ocular pressure. However, the resumption of drainage made possible by the lowered venous pressure in the exit veins, and possibly facilitated by the temporary increase in the intra-ocular pressure, quickly neutralizes this rise so that the same circulatory changes, effective at once in congestive glaucoma, eventually induce a fall in tension in simple glaucoma.

This explanation implies that the rise in intra-ocular pressure found in simple glaucoma is due to the suddenness of the sympathetic block and to the speed with which the capillary volume tends to increase. Were it possible to effect a gradual relaxation of sympathetic tone, it is probable that this preliminary rise in tension would not occur so that the intra-ocular pressure would fall slowly from the beginning.

After stellate ganglion block in congestive glaucoma the intra-ocular capillaries dilate in the same way as in simple glaucoma. There is a similar increase in the volume of the intra-ocular capillary bed which is compensated at once in the presence of a structurally open angle by a corresponding volumetric displacement of aqueous through the drainage channels, particularly the canal of Schlemm, this outflow being facilitated by a constriction of the pupil and by the lowered venous pressure in the exit veins.

In congestive glaucoma associated with an impediment to drainage, the effect on the intra-ocular pressure following sympathetic block depends upon the degree of obstruction. If the latter is incomplete, there is a preliminary rise (as in simple glaucoma) followed by a fall; but, where the obstruction is such that the fall in venous pressure is no longer effective in facilitating a rapid outflow of aqueous, the added capillary dilatation induces a rise of intra-ocular pressure which cannot be compensated.

It is to be borne in mind that the effect of blockage of the sympathetic

supply is only temporary since the circulation rapidly accommodates itself; procaine block of the stellate ganglion is therefore useless as a therapeutic measure even when the angle of the anterior chamber is open, and, as has been shown, when the angle is closed in congestive glaucoma it may be dangerous.

Summary

(1) The responses of the intra-ocular pressure in glaucomatous eyes to local procaine block of the stellate ganglion are recorded.

(2) In simple glaucoma there is at first a rise followed by a fall in intra-ocular pressure.

(3) In congestive glaucoma there is an immediate fall of intra-ocular pressure unless there is an organic obstruction to the outflow of aqueous. If the obstruction is partial, there is a preliminary and temporary rise followed by a fall; if it is complete there is a sustained rise of intra-ocular pressure.

(4) The findings are discussed and an attempt is made to account for them.

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POLARIZED LIGHT STUDIES OF CORNEAL STRUCTURE*

BY

E. J. NAYLOR

Department of Ophthalmology, University of Manchester

THE importance of the cornea as the major refracting surface of the eye and the peculiar circumstance of its transparency have given rise to investigations since early times. Recent work on the hydration properties of the cornea, for example that of Cogan and Kinsey (1942) and Hart and Chandler (1948), seems to indicate that the problem of transparency will be solved only by an attack over a wide field. It is also apparent from the literature that our knowledge of the fine corneal structure is still limited, and that comparatively little has been done to apply techniques other than that of visual microscopy. These include the use of the electron microscope, *x*-ray diffraction, and polarized light, all of which have been applied with success to the elucidation of the structure of other tissues. The literature contains reports of investigations of eye tissues by electron microscopy (Sebruyns, 1950) and of *x*-ray diffraction (Hertel, 1933), and a paper describing the use of an ultra-violet absorption technique for investigating corneal transparency (Caspersson and Engström, 1946). The relevant literature on polarized light is quoted by Cogan (1941), and has been briefly reviewed by Stanworth and Naylor (1950).

In the latter paper the phenomenon of the interference figure was discussed in terms of photo-elasticity and crystal optics. The qualitative results of this investigation together with some additional observations made by the present author have been further analysed (Stanworth and Naylor, 1952), and it has been shown that the coefficient of birefringence of the cornea is 0.0014. Considered as a lamina made up of a series of anisotropic fibres arranged randomly in layers parallel to the surface, the coefficient of birefringence of the constituent fibres, according to theoretical calculations, should be about 0·0028, *i.e.*, twice that of the lamina.

The term " birefringence " is often used in different ways, and various adjectives have been employed by different authors to connote specific meanings. In its widest sense it is synonymous with double-refraction or optical anisotropy in indicating that light travels at different speeds—and that, therefore, different refractive indices are found for the substance—according to the direction of travel and the direction of vibration of the incident light. When used quantitatively, " effective birefringence " indicates

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the difference between the ordinary and the extraordinary refractive indices for any direction of light path, and " coefficient of birefringence " indicates the maximum value of the birefringence, which occurs when the light is vibrating along the principal axes of the substance. A quantitative value for " birefringence " in what follows—and usually in the literature—implies the coefficient of birefringence.

It is the purpose of this paper to report some of the findings of an investigation originally designed to verify the above analysis experimentally, and later extended to include the application of techniques involving polarized light to studies of the submicroscopic structure of the corneal stroma. Details of the methods are published elsewhere (Naylor, 1952).

Microscopic Structure

Attempts to isolate a piece of corneal stroma in the form of a single fibre or lamella failed, and histological sections were therefore made by freezing or fixing techniques. Examination of these sections, typical photographs of which are seen in Fig. 1, confirm the findings of His (1856) that the corneal fibres are birefringent with optic (slow) axes along their length. In antero-posterior sections of the cornea, some fibre layers will be encountered in which the fibres have been cut perpendicular to their length, along their length, or in intermediate positions. The first-named will show no effective

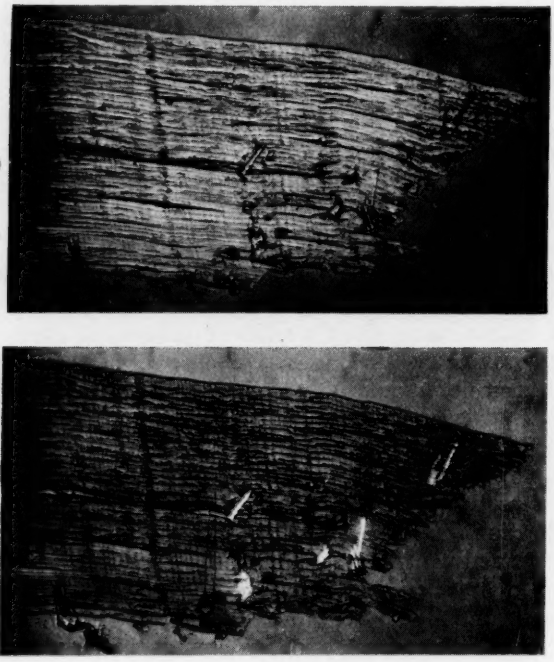

FIG. 1.—Antero-posterior section of cat cornea, 25μ thick, photographed under polarizing microscope with crossed polars and sensitive tint plate. × 80.
Specimen in diagonal position with slow axis of tint plate: (*a*) perpendicular to fibre direction, fibres appearing orange; (*b*) parallel to fibre direction, fibres appearing blue.

birefringence, since the light will be travelling parallel to their optic axis; the second type will show the maximum effect; the last-named will produce effects of varying magnitude according to their inclination to the plane of the section. It was thought that the course of the corneal fibres might thus be mapped out from readings of the retardation they produced, but the technique of measurement is not sufficiently delicate to enable this to be done with certainty. Nevertheless, large numbers of readings were taken on many sections cut in various ways and a statistical plot of these results showed no support for the suggestion put forward by Kokott (1938) of preferential orientation of fibres in layers at different depths in the cornea. It is not possible directly to measure the coefficient of birefringence (ω) but one can assess with accuracy the relative retardation (Δ) of the light components issuing from the doubly refractile corneal elements and it can be shown from first principles that $\Delta = d.\omega.\sin\alpha.\tan\alpha$, where α is the angle that the direction of passage of the light makes with the optic axis and d is the thickness of the section.

However, the coefficient of birefringence of the fibres was obtained from the maximum readings of the retardation, by dividing the latter by the thickness of the section. The most constant results were obtained with sections 15–25 μ thick, mounted in Ringer-Locke solution, and these gave a figure of 0·0030 for the coefficient of birefringence. This value is in accordance with the prediction of 0·0028.

Another interesting observation is that with the aid of polarized light about one hundred distinct zones can be counted in the cat cornea, compared with forty visible under ordinary illumination. This is not readily demonstrable in an illustration based on a single photograph, for what appears in the latter as a single zone of the same intensity may be resolved visually into two or more zones by a slight rotation of the polarizer or analyser. The human cornea is usually stated to contain about 60 lamellae; this figure was given by Bowman (1849) who, however, pointed out that no exact estimate could be given. It seems probable that this number is too low and that 150 would be a better estimate on this basis.

Sub-Microscopic Structure

The standard biological technique employed as a preliminary to polarization analysis of tissue structure is to immerse the object consecutively in fluids of different refractive indices and then measure the retardation. These values are then plotted with refractive indices as abscissae and coefficients of birefringence as ordinates to give a curve similar to that derived from the well-known Wiener relationship (see, for example, Schmitt, 1939). Such a curve indicates whether the tissue exhibits intrinsic birefringence due to molecular asymmetry, or form birefringence due to the regular arrangement of asymmetrical aggregates of molecules (micelles), or both; it also reveals the probable nature of the micelles and their refractive index. The standard

technique was not directly applicable to the cornea because of its isotropic appearance when viewed normally, and also because it was not possible to isolate individual fibres satisfactorily. A method was devised, however (Naylor, 1952) by which the retardation was measured for light passing obliquely through circular disks of cornea removed by means of a trephine punch and the birefringence of the constituent fibres computed therefrom. Over one hundred disks were examined from cat corneae from freshly enucleated eyes, and from eyes preserved in either 2½ per cent. formal saline, 5 per cent. mercuric chloride, or 35 per cent. alcohol. These corneal disks exhibited both form and intrinsic birefringence of positive sign, the values of the latter for the above categories being 0·000450, 0·000525, 0·000388, and 0·000250 respectively. The refractive index of the micelles was found to be between 1·50 and 1·52, which is low compared to that of most other physiological proteins, and calculations from the Wiener formula suggest that they occupy somewhat less than 3 per cent. of the total volume of the corneal substance. The presence of intrinsic birefringence denotes molecular asymmetry, and its positive sign indicates that the molecules have their long axes in the fibre direction. Form birefringence is due to the asymmetry of the molecular aggregates or micelles, and the finding that it has a positive sign indicates that the corneal micelles are of the rodlet type.

Intrinsic Birefringence.—In preparations which differ only in their degree of swelling, assuming no change in the orientation or in the birefringence of the molecule itself, the intrinsic birefringence should be inversely proportional to the volume. In the cornea practically all the swelling occurs at right angles to the plane of the fibres, and therefore the products of intrinsic birefringence and the thickness of the disks should be approximately constant. The mean figures for 27 disks fixed in formalin, fourteen disks fixed in mercury, and fifteen disks fixed in alcohol are $2{\cdot}68 \times 10^{-4}$, $2{\cdot}33 \times 10^{-4}$, and $2{\cdot}60 \times 10^{-4}$, for thicknesses of 0·52, 0·60, and 1·06 mm. respectively: it may be deduced, therefore, that swelling and fixation bring about no gross disorientation of the molecules. It is of interest to observe the values obtained for disks of different thicknesses, all fixed by the same method, but the range of thickness in the present experiments was not sufficient to allow this to be done except in the case of the fifteen alcohol-fixed disks, which varied in thickness from 0·76 to 1·33 mm. Divided into one group of three disks all with mean thickness 0·83 mm., and three groups of four disks with mean thickness 0·95 mm., 1·12 mm., and 1·27 mm. respectively, the corresponding figures for the products of intrinsic birefringence and thickness are $2{\cdot}80 \times 10^{-4}$, $2{\cdot}56 \times 10^{-4}$, $2{\cdot}72 \times 10^{-4}$, and $2{\cdot}22 \times 10^{-4}$. This does not suggest undue disorientation of the molecules, although the number of readings available is hardly sufficient to enable one to be dogmatic. (Correlation coefficient, r, between ω and $d = -0{\cdot}73$; probability integral, P, $= 0{\cdot}25$).

Form Birefringence.—Although the protein content of the cat cornea is about 25 per cent. (Duane, 1949), the calculated volume of the micelles from the present results is less than 3 per cent. A low value is not unexpected in such a highly aqueous structure as the cornea. Possible explanations, not mutually exclusive, are:

(*i*) that the major portion of the corneal protein may be in unaggregated molecular chains;

(*ii*) that the molecules may be aggregated into fringed micelles having boundaries less well defined than those in the ideal mixed body considered by Wiener;

(*iii*) that the micelles, though sharply defined, may not lie parallel to the long axis of the fibres.

Some support for the last supposition is offered by the electron microscope studies of Sebruyns (1950) who found a helicoidal arrangement of fibrils. The last two considerations lead to the deduction that 3 per cent. represents too low a value for the true micellar volume, and the electron microscope photographs by Sebruyns (1950), showing tracts inclined at angles of about 45°, indicate that the extent of the underestimate is not inconsiderable. The figure of 5 per cent. would probably be a better estimate as it yields a value of 0·008 for the micellar intrinsic birefringence (intrinsic birefringence divided by micellar volume). This accords well with that obtained for other protein micelles; for example, Bear, Schmitt, and Young (1937) found 0·005 for nerve axoplasm, and Weber (1934) found 0.008 for myosin.

The low value of the micellar volume could be due either to a large number of very small particles or to a smaller number of larger particles. These two types, of course, are both small with respect to the wavelength of light, and the polarization technique cannot distinguish between them. On the basis of *x*-ray diffraction studies, Hertel (1933) estimated the micellar size as about 1 mμ × 10mμ; there would thus be about 5×10^{15} per cubic millimeter of cornea.

If the micelles remained unchanged during swelling of the cornea, the experimental results might be expected to show that the product of micellar volume (expressed as a fraction of the total volume) and thickness remained constant. The respective mean values for disks fixed in formalin, mercury, and alcohol, however, are 0·0156, 0·0180, and 0·0239, for mean thicknesses of 0.52 mm., 0·60 mm., and 1·06 mm., which suggests that the size of the micelle increases during swelling. The swelling of the cornea, then, is at least partially intra-micellar, a finding which agrees with *x*-ray diffraction observations on collagen (Küntzel and Prakke, 1933), and on the cornea (Hertel, 1933). The above figures indicate that for an increase of 100 per cent. in thickness the micelles swell by about 50 per cent. in the fixed cornea, a figure which may be greatly increased in fresh material or in the living state. If the absorbed fluid had its normal refractive index of about 1·34, it might be expected that such a swelling would result in a fall in the refractive index of the micelles to about 1·45 (according to the law of Gladstone and Dale, 1863). Such an effect was not observed. There is, however, no evidence that the formula of Gladstone and Dale applies to intra-micellar changes. Indeed, these authors quote experiments in which the formula failed to apply when hydrates were formed, and it would be surprising if no such effects occurred in the submicroscopic spaces involved in these changes. In addition, the concept of a hydration layer, which will be put forward later, involves the assumption that in such circumstances the fluid has a higher density and hence a higher refractive index than 1·34, and consequently that the value of the micellar refractive index to be expected is not calculable.

Schema of Corneal Structure

It may be helpful, in conclusion, to put forward a schema of the sub-

microscopic and microscopic anatomy of the corneal stroma in order to introduce a terminology for its constituent parts; if generally adopted this would avoid the uncertainty which often exists at present. The cornea consists chiefly of collagen, the molecules of which, like those elsewhere in the body, consist of long chains, running, in general, parallel to the length of the fibrils which are about 0·3–0·6 μ in diameter (Caspersson and Engström, 1946). Within the fibril some of the molecules are aggregated together to form micelles (Fig. 2), there being a continuous range in size of the water-holding spaces between the molecules in the intra-micellar regions ranging from about 1 mμ upwards (Frey-Wyssling, 1948). The fibrils themselves are aggregated together to form fibres which run parallel to their neighbours at the same depth in the cornea, but which cross at an angle to those more superficial or more deep thus forming sheets parallel to the surface. It is proposed that the term lamellae be reserved for these sheets of fibres of which there are about one hundred in the cat cornea, each about 5 μ thick. The spaces between the fibrils in any one fibre, and even between the fibres in any one lamellae, may be merely large spaces of the same type as are found in the interior of the fibril. This would account for the markedly homogeneous nature of the lamellae in corneal sections examined by ordinary microscopy. The spaces between any two lamellae, however, are probably of a fundamentally different nature. The fibres in different lamellae will arise from different cells in the process of development, whilst those in any individual lamella may often arise by a process of division from the same cell. This accounts for the relative ease with which the cornea may be split along the lamellar boundaries in corneal surgery. The directions in which the fibres run in successive lamellae are such as to form a random distribution for the cornea as a whole. It is as if the embryonic cornea was formed originally from a few random cells at different depths, which, by a process of lateral division presumably conditioned by the rising intra-ocular pressure, give rise to the sheets of fibres we now distinguish as lamellae.

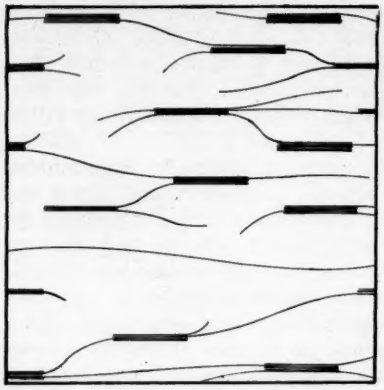

FIG. 2.—Diagram of interior of corneal fibril showing long chain molecules and micelles.

In order to consider the relationship of the structure to the property of transparency, it is essential to know the refractive indices of the various components. That of the micelles has been found to be 1·50–1·52; it must

be pointed out again, however, that this figure is based on a formula which postulates small particles with sharp boundaries, whereas micelles of the fringed type will have more gradual boundaries. It is probable, then, that this figure underestimates the refractive index in the centre of the micelle. In estimating the amount of scatter of light from such a particle no formula is available, the only comparable one being that of Rayleigh for isotropic spherical particles, conditions which do not obtain here. Nevertheless, it seems probable, that, as in Rayleigh's formula, a larger particle, within the limits of size under consideration, would tend to give more scattering. The high transparency, therefore, indicates that the micelles are extremely small.

The second boundary at which light loss might take place is that of the fibril. In discussing the light loss at this boundary, Caspersson and Engström (1946) have taken as a basis for calculations a refractive index of 1·385 for the fibril and one of 1·355 for the surrounding fluid; they have shown that if the transition were abrupt the substance should be completely opaque. They therefore postulate that the transition of refractive index is gradual. It should be pointed out that the figure of 1·385 for the refractive index of the fibril is a doubtful one. All methods of direct measurement of the refractive index of the corneal substance, whether on pieces of cornea or on corneal sections, must involve much larger elements than the fibrils. In structures of this size, the resultant value will be approximately a combination of the refractive index of the fibril and that of the inter-fibrillar fluid according to the admixture formula of Gladstone and Dale (1863), checked for protein solutions by Adair and Robinson (1930). Since the refractive index of the fibril will be underestimated, the argument of Caspersson and Engström still stands. It seems possible that the solution to the problem of the possible cause of this gradual transition lies in the fact that the fibril is of a size just sufficient to involve the formation of phase boundaries (Frey-Wyssling, 1948). In this case one might expect a hydration layer of increasing density of water molecules as the core of the fibril is approached (Fig. 3), and the refractive index at the edge of the fibril may then have a gradually increasing value towards the core. Some such arrangement might be expected to occur at the fibre boundary.

FIG. 3.—Diagram of molecular hydration layer associated with corneal fibril.

It is of some interest and importance to consider how fixatives may alter the transparency. Since the results from these studies in different fixatives can be largely explained on the basis of alterations in degrees of swelling, and the birefringence of the cornea is unaffected by fixation, it appears that the fixatives do not greatly disturb either the molecular chains or the micelles. The opacity they usually produce must, therefore, be related primarily to

the phase boundaries. This is not surprising, particularly in the case of alcohol which is a markedly hydrophilic and surface-acting substance. It is possible that alcohol disturbs the hydration layer and causes the formation of a sharp boundary, a process analogous to coacervation. The conditions are then, as Caspersson and Engström have proved, such as to cause much light scatter. The fact that the alcohol-fixed cornea becomes maximally transparent when immersed in fluids of refractive index 1·54–1·58 (Aurell and Holmgren, 1946) indicates that the resultant alcohol-fixed fibril has a refractive index of this value. It does not, of course, indicate that this is its value in the normal state.

Summary

The corneal stroma of the cat has been investigated by polarized light techniques adapted for the purpose. It is suggested that a small proportion (say, 5 per cent.) of the long-chain molecules form extremely small micelles, the nature and distribution of which are discussed; these have the (comparatively) low refractive index of 1·50–1·52. These aggregated and unaggregated molecules make up the corneal fibrils, around which lie hydration layers of varying density; bundles of these fibrils constitute the corneal fibres which form about one hundred layers (lamellae) each about 5 μ thick. No evidence has been found of any preferential orientation of fibre directions in different lamellae. The origins of the interfibrillar and interlamellar spaces are considered and the effects of swelling and the relationship of the structure to transparency in the fresh and fixed cornea are discussed.

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PRESENT STATUS OF CORTICOTROPIN (ACTH), CORTISONE, AND HYDROCORTISONE IN OPHTHALMOLOGY*†

BY

DAN M. GORDON, JOHN M. McLEAN, AND HERBERT KOTEEN

From the Departments of Surgery (Ophthalmology) and Medicine, New York Hospital, Cornell Medical Center

In previous communications (Gordon and McLean, 1950; McLean and others, 1951; Gordon and others, 1951) this group has reported its experiences in the treatment of ocular disease with the use of corticotropin (ACTH) and cortisone. The present paper summarizes our knowledge of the clinical use of corticotropin and cortisone in ophthalmology and adds experiences with hydrocortisone during the past year.

Nearly 3 years have elapsed since the introduction of these hormones into the ophthalmic armamentarium, but acquaintance with their uses, abuses, and limitations is not yet universal. Most ophthalmologists have had experience with the topical application of cortisone in drops or as an ointment, and many have used it systemically by intramuscular injection and orally in tablet form, but comparatively few have employed corticotropin. Too many physicians are still afraid to use corticotropin, or even cortisone by injection; but they occasionally use cortisone orally because they have the naïve belief that anything given by mouth cannot be very dangerous.

A recent survey conducted for one of the manufacturers‡ by an independent testing company indicates that only 2 per cent. of ophthalmologists are familiar with the use of corticotropin. Even allowing for a great error in this analysis the final percentage would remain relatively small. One of the chief reasons for not using this potent hormone is the fear of the side-effects which systemic medication may produce. This same fear has undoubtedly militated against the use of cortisone systemically where systemic therapy has been indicated; or has resulted in the use of inadequate doses.

It is unfortunate that the therapeutic horizon of too many ophthalmologists ends with the use of cortisone by topical application. While the topical applications of cortisone are very efficient, where indicated, they are equally impotent where not indicated, and an excellent mode of therapy may be discredited by improper use.

The use of cortisone topically as the primary procedure in treating superficial ocular disease is usually highly efficient. Cortisone drops or ointments are at times valuable in the initial treatment of uveitis, but one cannot count

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‡ Armour Research Laboratories.

on their being consistently successful in intra-ocular disease. In many cases where the disease has responded to intensive treatment with subconjunctival cortisone or systemic corticotropin or cortisone, the topical applications may then prove valuable in the secondary control of the disease.

As a rule there is some intra-ocular absorption of topically applied cortisone. Sometimes this amount is insufficient to control an acute intra-ocular disease, but may suffice in the secondary control.

Subconjunctival injections of cortisone, with or without support by topical applications are often sufficient in anterior uveitis, and less frequently so in posterior segment disease, and in both, as noted later, an initial short course of systemic therapy may be valuable or essential.

In the treatment of inflammatory disease of the posterior globe or of severe anterior segment disease which has not responded to topical or subconjunctival cortisone, systemic therapy is certainly indicated. If the patient is receiving ambulatory treatment, oral or intramuscular cortisone or intramuscular injections of corticotropin in the new long-acting vehicles are very useful. The new "gel" forms of corticotropin lend themselves to ambulatory use, as each injection is effective for at least 24 hours. It must be emphasized that many of the conditions which were formerly considered suitable for hospital treatment only, can now be handled on an ambulatory basis, if arrangements can be made for the patient to receive injections at home from a member of the family or a visiting nurse.

If the patient requires hospitalization the use of corticotropin in a prolonged intravenous drip is the most efficient weapon available (Woods, 1952). According to Thorn (1952), 25 mg. corticotropin administered intravenously in an 8-hr. drip is equivalent to 300 mg. cortisone.

The medical and lay public have been unduly frightened by some of the statements regarding complications which have been publicized. It was brought out at the Third ACTH Conference (Gordon, 1952; Smith, 1952; Wolfson, 1952) that healthy individuals suffering from a disease of an isolated organ such as the eye do not tend to develop the more serious complications (such as gastro-intestinal perforations) which are seen in a relatively small percentage of patients suffering from systemic illness. In the past ophthalmologists have had little experience with therapeutic agents having systemic as well as local effects but now, unless they take the trouble to study these compounds in co-operation with a specialist in internal medicine, they may deprive their patients of many of the advantages of present-day therapy.

These hormones are most efficient in the treatment of ocular disease when they are employed very early during the stage of acute inflammation. The compound selected should be given promptly and in doses large enough to meet the situation. There is apparently a definite relationship between the severity of the disease process and the amount of corticotropin or cortisone necessary to overcome it. It is possible to meet an inflammation of such

severity that neither corticotropin nor cortisone can achieve the desired result, but one cannot admit failure in any given case until both hormones have been tried by various routes. Further, as more potent preparations are becoming available, fewer failures should occur. The following case history illustrates this point.

Case Report

A male patient with acute optic neuritis of 3 weeks' duration was admitted on March 4, 1952, with vision of light perception superiorly in the right eye and 20/15-2 in the left. In June, 1950, he had had a similar loss of vision on the right, with later loss of vision on the left, followed by improvement in both eyes. He is a suspected but unproved case of multiple sclerosis. He was placed on intravenous corticotropin, 25 mg. daily for 7 days, increased to 50 mg. daily for an additional 6 days. Vision in the right eye was then 3/200. In the interim vision in the left eye had regressed to 20/40 as this disk began to assume the typical picture of optic neuritis. The corticotropin was discontinued and cortisone given in doses of 50 mg. every 6 hrs, for 2 days. His vision now was counting fingers at 3 feet, 20/40. The authors had just been requested to supply data on a new preparation of corticotropin in a long-acting vehicle, which the manufacturer thought more potent than those then being used by our group. The patient was given 40 units of this preparation twice daily, for 10 days, when the dose was halved for 2 days and then reduced to 10 units, twice daily, for 2 more days before being discontinued. On the second day his vision was 3/70 in the right eye, improving to 20/160 by the third, 20/70 on the sixth, 20/40 on the ninth, and 20/30 on the eleventh day. The vision in the left eye remained at 20/40 until the ninth day on the new preparation when it was recorded at 20/30, uncorrected. This patient has not relapsed (as at June 1, 1952).

It is recognized that these agents do not affect the underlying cause of the disease; and are at their best when employed in the treatment of acute self-limiting conditions. Prompt and judicious use of corticotropin or cortisone in the treatment of an acute ocular disease or allergic reaction will usually result in the subsidence of the inflammation and thus prevent destruction of vital ocular tissue. Meanwhile the pathogenic process burns itself out. Failure to continue the hormone long enough for the acute pathogenic process to run its normal course will result in relapses demanding reinstitution of therapy. Fear of either corticotropin or cortisone by the physician who regards them as drugs of last resort, to be used only when everything else has failed, often means that the disease process is given time to become chronic. The patient is now faced with a long, or even permanent, period of treatment, whereas the disease could possibly have been aborted rapidly had hormonal treatment been instituted at its onset. An analysis of failures with hormonal-steroid therapy makes it clear that most of these are due to " too little ", or " too late ", or both.

Nor should the advent of corticotropin and cortisone be a signal to discard all previous agents employed in the handling of inflammatory eye disease. Some of these may serve to speed up the convalescent period so saving the amount of hormone employed. Atropine, fever therapy, and antibiotics continue to have a prominent place in the treatment of ocular disease, when indicated.

Atropine certainly still merits use in the treatment of the uveitides, putting the eye at rest, and making examination easier.

Randolph and Rollins (1950), Arendshorst and Falls (1950), and Rosen (1952) have shown that artificial fever therapy apparently functions at least partially *via* the release

of adrenocorticotropic substances. There seems to be no real reason for using fever therapy simultaneously with corticotropin or systemic cortisone, but the two methods can be employed on alternate days where the patient seems to be developing hormonal side-effects (moon-face, etc.). Again, a course of fever therapy can be employed as part of the tapering off process at the end of a course of corticotropin or cortisone or as part of maintenance therapy in a chronic inflammatory disease.

Either corticotropin or cortisone may prove excellent in the treatment of the inflammatory phase of eye infections without any appreciable effect upon the causative organisms which continue to be present. Conversely the indicated antibiotic often fails to clear up the symptoms of disease. A combination of the hormone, which suppresses the inflammatory reaction, and the antibiotic, which "sterilizes" the area, frequently gives an excellent visual result and may shorten the period of convalescence.

It has been demonstrated (Leopold, 1951) that certain antibiotics (*e.g.*, penicillin) will not penetrate the ocular tissues in appreciable quantities in the presence of normal capillary permeability. When this is altered as in ocular inflammation these antibiotics will be found in concentration and can function therapeutically, but since they suppress the ocular inflammation and cause a return to normal capillary permeability, they cease to be able to enter the ocular tissues. Certain other antibiotics such as chloramphenicol, however, are exceptions to this statement. Therefore, in the presence of severe ocular infection where the use of antibiotics is desirable, either one must not employ corticotropin or cortisone or one must use with them an antibiotic which will continue to be effective in their presence.

Either corticotropin or cortisone may produce a similar therapeutic result in the average case of ocular inflammation or allergy, but since these are two very different compounds functioning *via* two different mechanisms, they may produce different results in the same patient.

It was thought formerly that corticotropin functioned primarily through the stimulation of cortisone-like substances, but it is now apparent as a result of the work with hydrocortisone that this is not entirely the case. By virtue of the fact that it stimulates the entire adrenal cortex and other structures as well corticotropin has a much broader spectrum of action than cortisone. Therefore, if either fails in the treatment of any eye disease, one must not assume that the other will fail also. On the contrary, such failure is to be regarded as a signal for the use of the alternate compound.

It is our practice at the New York Hospital to give an acute case of ocular inflammation a trial period of not more than 48 to 72 hrs on the hormone previously selected. Experience has indicated that in the average case a beneficial response will be noted within 24 hrs, but if a good response is not seen within 72 hrs, it is assumed that the patient is either not receiving enough of the hormone or is a subject for the alternative hormone. If he is on a moderately low dose, the amount is increased. If this fails, or if he is already on a large dose (*e.g.*, 300 mg. cortisone daily), he is switched to the other compound.

In all cases the measurement of the circulating eosinophils and the response of the disease process are the chief guides to dosage, subject to the appearance of side-effects. These last have been discussed at such length in the literature that it suffices here merely to enumerate them (Table I, opposite). As our experience with these compounds systemically has increased, fewer and fewer complications have been noted. It is obvious that this is the result of improvement in management and in ability to note the onset of side-effects early.

Treatment of Chronic Disease

When one meets with a chronic inflammatory disease or has permitted an acute disease to become chronic, a different situation results. Experience has shown that the chronic inflammatory or allergic eye disease cannot be

TABLE I

IMPORTANT MEDICAL ASPECTS OF POSSIBLE SIDE-EFFECTS

Complications of Systemic Therapy	Management
Retention of sodium chloride and water	Weigh daily; if sudden increase in weight is noted, restrict salt and/or use diuretics
Marked elevation of blood pressure	Follow daily pressure; if severe continuing hypertension is present therapy may have to be stopped
Low serum potassium and hypochloraemic alkalosis	Follow EKG for potassium changes and serum for changes in CO_2 and chlorides; oral potassium chloride (3 g. daily) prevents these changes usually
Hyperglycaemia and glycosuria	Important in diabetics and suggests need for more insulin
Major psychotic changes	Watch for manic, depressed, schizoid alterations; if severe, stop therapy
Signs of Cushing's disease: acne, hirsuitism, plethora, striae, fat pads	These disappear on termination of hormonal therapy and are no contraindication
Pigmentation of skin and nails	A rare, cosmetic problem of no consequence
Anaesthetic reaction (reduction in pain threshold)	Rarely, there may be painless perforation of a viscus without fever; locate air below diaphragm and operate

aborted completely by hormonal treatment, for when the treatment is stopped the disease will shortly return. Occasionally however a long period of remission will occur. Whether it would have also occurred spontaneously at the same time is not always certain. However, the use of either one of these compounds during the chronic or recurring phase will, when successful, prevent the occurrence of damage. Since many chronic diseases tend to have remissions it behoves the ophthalmologist to protect the chronically inflamed eye as far as possible pending the onset of such a remission. Further, in these days of rapid advances in therapy one never knows when some superior method of treating chronic diseases will be found. Should such an event ensue, the eye which has been kept in an optimal condition, will be in the best position to be benefited. In our experience relapses require less hormone over a shorter period in order to produce a remission. This is contrary to the experience of Duke-Elder (1951).

The management of chronic inflammatory or allergic eye disease is very difficult. The regime here is based on the principle that, once the severe manifestations of the inflammation have been suppressed by intensive systemic treatment, they can be held in a state of suppression, frequently by less intensive therapy. The ideal case would be one which could be controlled by topical cortisone, after initial suppression by systemic therapy. Unfortunately, such cases are rare. It is our usual practice to hospitalize the patient with chronic inflammatory disease and to give him a course of

ACTH by intravenous drip, the length of hospitalization being regulated by the patient's response. Once the severe symptomatology has subsided, the dosage is tapered off, and measures are instituted to render him ambulatory. The next step is to work out a maintenance dosage harmonizing the maximum safety for the patient and the minimum damage to the eye, that is the least amount of the indicated hormone and the maximum interval between treatments. If the chronically affected eye can continue safely with local therapy alone that is obviously the procedure of choice, but we have found that many such patients require systemic therapy, at least early in the course of treatment, either with corticotropin in one of the long-acting vehicles or with cortisone. The newer forms of corticotropin in long-acting vehicles lend themselves especially well to ambulatory treatment, as does cortisone orally. We have not hesitated to bring the patient back into the hospital for an occasional week-end of intensive intravenous corticotropin therapy and we have also employed fever therapy as an adjunct to the treatment of chronic eye disease. In some cases which seemed to fit our concept of ocular tuberculosis, isonicotinic acid was used. It is still too early to comment on the results of this therapy which had seemed promising in at least two cases, despite later relapses. Some of our long-term chronic cases have shown a need for less and less medication after long periods on hormonal therapy. This treatment is too new for anyone to be sure whether a chronic inflammation will or will not burn itself out on long-term treatment but one should do one's best to preserve these eyes as long as possible. Some of our patients who have been treated successfully for 1 or 2 years have only one eye.

Woods (1951), and Woods and Wood (1951) have reported on the deleterious effects of these agents when employed in the treatment of experimentally produced ocular tuberculosis with one possible qualification. These results have not been duplicated in our clinical practices. A small number of cases have done poorly when treated with local or systemical cortisone, but nearly all of them responded well to corticotropin. The whole question of the relation of these two hormones to tuberculosis, either local or systemic, has yet to be resolved. Apparently, the available evidence indicates that corticotropin is safer than cortisone in the presence of tuberculosis, but that neither is as yet proved to be clinically dangerous (Tompsett, 1952).

The numerous case reports in the literature render it unnecessary to include any statistical analysis here. Woods has compiled the findings at both the New York Hospital and Johns Hopkins Hospital (Wilmer Institute), and has commented on the marked similarity in results. Other large series, such as those of Duke-Elder, show similar trends.

Much of the earlier literature is very confusing and paradoxical because most papers were based on relatively few cases. Some failures were due to the fact that only local cortisone was used, and others to the relatively

minute doses or to the lateness of the institution of hormonal therapy. The failure to use potassium chloride together with systemic medication caused many side-effects. Occasionally, an insufficiency of potassium will result in retinal oedema with a decrease in vision in the presence of sufficient hormone. Potassium chloride can be used in doses up of to 12–15 g. daily. The present trend is towards increasingly large doses of this salt. The indication for the early use of either corticotropin or cortisone is any acute inflammatory or allergic disease of the eye or ocular adnexa, for which specific therapy is not available. Where specific therapy is indicated, as for example in syphilitic infection, it may be employed either alone or in conjunction with hormonal therapy.

The retardation of healing said to be caused by both corticotropin and cortisone, has been over-dramatized, since, in most cases, the amount of hormone employed experimentally exceeded that generally used in ophthalmic therapy. Where healing is a factor, it is probably best not to use cortisone or corticotropin until about 10 days after intra-ocular surgery. However, if one is trying to prevent the scarring down of a bleb in a filtering operation, then early judicious use of local cortisone is indicated, as also in unusually severe post-operative reactions. A number of patients have had ocular surgery while receiving corticotropin or cortisone (Thorpe, 1951) without any apparent interference with healing. The present authors have seen one temporary delay in healing after starting topical cortisone on the third post-operative day; when the cortisone was discontinued the wound healed without further delay or complication. However, it is wise to remember the possibility of a delay in healing and to use precautions, such as extra sutures, etc. In the treatment of chorio-retinitis certain cases will heal with a " smear " instead of the usual clean cut scar, and will practically always have recurrences some time after the cessation of treatment. Relapse may be prevented by prolonging the course of therapy with either subconjunctival or systemic treatment, or by employing artificial fever. The treatment here should be continued until a pigmented or " hard " scar is obtained.

One of us had the opportunity of seeing a small number of cases of severe corneal ulceration due to pseudomonas infection thought to have been traced to contaminated solutions of cortisone. In all but one of these cases, the patient was immediately taken off the cortisone and put on antibiotic therapy, and all did poorly. The one exception was hospitalized and treated with a different mixture of cortisone in addition to antibiotics, and this was the only patient who did well. The combination of the indicated antibiotic with hormonal therapy is often superior to either agent alone.

We have used cortisone and sodium sulphacetamide* for the past year; and have found it efficient. The sulphacetamide serves a two-fold purpose:

(*i*) It combats infection.

(*ii*) It serves to render the solution sterile.

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* Supplied by the Schering Corporation.

Technically, the sterilization of cortisone " drops " has proved difficult, but the addition of an antibiotic serves to prevent contamination.

The authors have also employed combinations of cortisone and an antihistaminic* ("Chlor-Trimetron") in local allergies. The addition of the antihistamine has made it possible to use weaker solutions of cortisone (0.25 per cent.), and the combination has proved successful.

Perhaps the chief contraindication to the use of these agents in ocular inflammatory disease is infection with the various viruses. Here for the most part results have been poor, with only a very occasional good. These agents have very little, if any, influence in either direction upon the bleeding retinopathies such as diabetic retinopathy and Eales's disease. One of our two cases of Eales's disease treated with corticotropin felt that she afterwards had a longer period of freedom from ocular bleeding. The same patient had profuse ocular bleeding after two different trial weeks of oral isonicotinic acid therapy.

Experimental Observations

Corticotropin and cortisone differed from the many new therapies in that considerable clinical experience was accumulated before much laboratory data was available. The latter is now beginning to corroborate and explain most of the clinical results, though much remains to be done.

All ocular inflammations are accompanied by an increase in capillary permeability, which is an important feature of the exudative process. These hormones do not affect capillary permeability in the normal eye, but in the inflamed eye have the power to reduce it to normal (Ashton and Cook, 1951; Cook and MacDonald, 1951; Leopold and others, 1951), which helps to explain the dramatic response of the acutely inflamed eye to these compounds. In wounds in experimentally treated animals practically no exudate and fibrin is seen 24 hrs after wounding or the application of croton oil (Michael and Whorton, 1951). Biegel (1951) produced horse serum uveitis in rabbits and noted that cortisone inhibited the formation of plasmoid aqueous and fibrin in the anterior chamber.

Selye (1950), Woods and Wood (1951), Biegel (1951), and other workers have shown that these compounds have a marked inhibitory effect upon experimentally produced allergic and inflammatory reactions. Certain substances will produce such reactions in untreated experimental animals, but no such reactions occurred when they were first pre-treated with hormones. Woods and Biegel have each demonstrated that the hormones block the result of antigen-antibody reaction in ocular tissue.

The present authors have reported on a similar clinical case. The patient was a boy with confirmed sympathetic ophthalmia, who was given an uveal pigment skin test while under treatment with corticotropin; when the injected area of skin was eventually biopsied no cellular reaction was noted.

* Supplied by the Schering Corporation.

Cortisone also inhibits corneal neovascularization. Clinically, this is best demonstrated by subconjunctival injections of approximately 8 mg. cortisone at the sites of the new vessels. Topical applications were effective, and same results were obtained with hydrocortisone.

Leopold and others (1951) demonstrated that cortisone inhibited corneal epithelial regeneration, after the production of standard abrasions. The present authors were first stimulated to use cortisone topically in ocular disease by the reports of Baker (1949) and Baker and Castor (1950), to the effect that cortisone prevented regrowth of hair when applied to the skin of rats. Various reports concerning the action of cortisone on wound healing and mitosis have been somewhat at odds with each other, on account of variations in dosage; when large concentrations were used healing was retarded, but with moderate amounts this result was not significant.

Ashton and Cook (1951) and Lister and Greaves (1951) found that cortisone in small doses did not appreciably retard epithelial regeneration in standard corneal abrasions, but that there was inhibition with larger doses. They did find a decrease in endothelial regeneration of rabbits' corneae under cortisone, but it did not seem marked enough to be important.

In animals it has been demonstrated that the formation of connective tissue in wounds and inflammations is delayed by cortisone, and that thus healing is retarded (Plotz and others, 1950; Ragan and others, 1950). Similar observations in man have been contradictory and showed less delay; the dosage used in the experiments was far greater than that used clinically.

Steen (1951) has shown that when cortisone was employed in a concentration equal to 25 times that used clinically there was no inhibition of mitosis or growth in tissue cultures.

Related Compounds

Our experiences with △-5-pregnenolone and 21-acetoxypregnenolone in a series of 31 cases with degenerative and inflammatory ocular disease failed to demonstrate any activity on the part of these two compounds.

The melanophore hormone has been employed in our clinic in a series of patients with either retinitis pigmentosa or diabetes. As will be reported in a separate communication, we failed to obtain the dramatic results reported by Steffensen and Kukora (1951) or Gonzalez Vanrell and others (1949).

The recent findings commented upon in the *Journal of the American Medical Association* (1952) that placental tissue and extracts possess adrenocorticotropic activity remind us of previous experiences with "tissue therapy" (Gordon, 1947; 1948)

Hydrocortisone

17-hydroxycorticosterone (Compound F), the newest of the steroid hormones to be introduced to ophthalmology, is used both as an acetate and in the free alcohol form. Though the authors have used it for almost a year, they feel that the range of application is not yet complete.

Hydrocortisone has been employed in a series of sixty cases much in the same manner and in the same dosages as cortisone; in 0.5 and 2.5 per cent.

suspensions topically, 15 mg./g. as an ointment, 8⅓–12½ mg. subconjunctivally, and 100–125 mg. intramuscularly or orally daily. Systemically it appears to be more effective than cortisone in lesser concentrations (Alpert, 1952). Topically, its analgesic effect is the same or greater than that of cortisone. Administered subconjunctivally, it provokes less local reaction than cortisone. The acetate crystals remain in the subconjunctival space for a much longer period than cortisone and the free form absorbs overnight; both forms cause a local reaction similar to cortisone.

Vernal Catarrh.—Topically, hydrocortisone acetate has proved far superior to cortisone in three cases:

(1) Relapse occurred within 1 or 2 days in one of these patients after withdrawal of cortisone (topical and oral), but on the two occasions when hydrocortisone was used did not occur until 10 and 14 days respectively. This patient (a boy) required topical plus oral cortisone for good control, but a similar response was obtained with topical hydrocortisone alone.

(2) A second boy had previously been treated unsuccessfully with topical and systemic cortisone, as well as beta irradiation; his response to topical hydrocortisone used in drops and ointment was excellent, but relapse occurred four days after withdrawal.

(3) The third patient, who had not had cortisone previously, responded rapidly to topical hydrocortisone.

Local Lid Allergy.—Five cases responded promptly to topical applications of hydrocortisone acetate. A very severe case of more widespread allergy involving the face and extremities responded promptly to intramuscular injections of 125 mg. hydrocortisone acetate, but concentrations of less than that amount were ineffective.

Uveal Tract Disease.—Our first series included eleven cases treated with hydrocortisone acetate. The paradoxical results precluded any definite conclusions.

(*a*) *Anterior Uveitis.*—Two patients with iridocyclitis and one with low grade choroiditis were benefited by topical applications.

A fourth with a peri-vasculitis was improved by subconjunctival injection.

A patient with acute choroiditis involving the periphery had a drop in vision from 20/20 to 20/70 after a subconjunctival injection of hydrocortisone acetate, but had a prompt rise to 20/30 after a subconjunctival injection of the same amount of cortisone. Later, subconjunctival cortisone failed to maintain the improvement, and her vision again decreased. At this point she was hospitalized and given a course of intravenous corticotropin and her sight improved.

Two other cases of anterior uveitis continued to progress despite applications of topical hydrocortisone, but one of these improved markedly and the other moderately with corticotropin. The former had previously failed to respond to 2 weeks' therapy with cortisone drops at another clinic.

(*b*) *Chronic Posterior Uveitis.*—Four cases were treated with subconjunctival injections of hydrocortisone acetate. The results were so slight that evaluation is difficult. One of them, who had had uveitis for over a year had been subjected to various forms of treatment, including cortisone topically and systemically, artificial induction of fever, corticotropin intravenously and intramuscularly, and isonicotinic acid. He had always become worse when given cortisone by whatever route, but corticotropin controlled the inflammation when given in maintenance doses once or more weekly. He had a questionable mild improvement after the combined subconjunctival and topical use of

hydrocortisone acetate. He has recently been placed upon subconjunctival injections of free alcohol hydrocortisone, and his vision has improved from 20/50 to 20/30, with definite clearing of the vitreous. The beneficial effect of each injection of free hydrocortisone usually lasts about 3 weeks.

The free alcohol form was used in seven cases of chronic uveitis and in two cases of acute macular choroiditis. The two last mentioned responded immediately to the first subconjunctival injection of 8¼ mg. Three of the seven chronic cases are well controlled by subconjunctival injections, and a fourth by oral doses (having had a questionable response to subconjunctival injections). A fifth case (who has Boeck's sarcoid) was improved by the subconjunctival injections. A sixth case (whose uveitis is associated with erythema nodosum) exhibited no response to the first subconjunctival injection and was placed on intravenous drips of corticotropin, to which he responded well. In the seventh case no improvement was seen after subconjunctival injections.

On the basis of this small series the free form of hydrocortisone appears to be superior to the acetate form in the treatment of uveitis. Since the effects of the free alcohol form are seen rapidly and last but a few days, and the acetate form acts more slowly over a longer period, the next step will be to try a mixture of both.

Orbital Pseudotumour.—One patient, whose successive attacks have responded to both corticotropin and cortisone employed systemically, has exhibited an excellent response to the free alcohol hydrocortisone taken orally. The initial dose was 100 mg., rapidly reduced to 25 mg., daily.

The response of various conditions to hormone therapy is set out in Table II, where an attempt is made to reconcile the results described in the literature.

TABLE II

RESPONSE OF CERTAIN EYE DISEASES TO STEROID HORMONE THERAPY

Reaction	Condition	
Response	Lid allergies Keratitis (superficial, non-specific) Keratitis (herpes zoster, disciformis) Keratitis (acne rosacea) Keratitis (interstitial) Keratitis (striate) Keratitis (hypopyon) Marginal ulcers Some chemical burns	Acute and subacute uveitis Episcleritis Scleritis (early) Phlyctenular kerato-conjunctivitis Vernal catarrh Orbital cellulitis Orbital pseudotumour Optic and retrobulbar neuritis Central serous retinopathy
Response followed by relapse ...	Chronic inflammations of all ocular tissues	Chronic allergies
Paradoxical Results (evaluation difficult)	Keratitis profunda Eales's disease Stevens-Johnson syndrome Mooren's ulcer	Exophthalmos (various aetiologies) Branch venous thrombosis Secondary glaucoma Ocular pemphigus
	Herpes simplex (dendritic ulcers)	
No Response ...	Diabetic retinopathies Retrolental fibroplasia Scars Central vein thrombosis Deep scleritis	Degenerations—dystrophies Retinitis pigmentosa Cataract Primary glaucoma Optic atrophy
	Certain virus infections of the globe	

A suggested order of choice of hormones in various pathological conditions is shown in Table III, and dosage schedules that have been found efficient are set out in Table IV.

TABLE III

SUGGESTED ORDER OF USE

Condition	First	Second	Third
Generalized Inflammation	Corticotropin	Systemic cortisone	—
Lids	Topical hydrocortisone*	Systemic corticotropin or cortisone	—
Vernal Catarrh	Hydrocortisone	—	—
Cornea—Sclera	Topical cortisone (possibly preferably hydrocortisone)	Subconjunctival cortisone	Systemic corticotropin or cortisone
Uveal Tract			
(1) Anterior	Subconjunctival cortisone (topical in mild cases)	Systemic corticotropin or cortisone	—
(2) Posterior (Choroid)	Subconjunctival cortisone (mild)	Systemic corticotropin (severe)	Systemic cortisone
(3) Severe Uveitis (also Granulomata)	Corticotropin (intravenous preferably)	—	—
Sympathetic Ophthalmia	Corticotropin (intravenous preferably)	—	—
Optic Nerve	Corticotropin (intravenous preferably)	Cortisone	—
Chronic Disease	Local cortisone (possibly preferably hydrocortisone)	Corticotropin, in long-acting vehicle	Combinations of cortisone locally and corticotropin in long-acting vehicle, or cortisone systemically

* Judging from results to date it would seem that hydrocortisone may ultimately replace cortisone.

TABLE IV

DOSAGE SCHEDULES

Corticotropin	*Intramuscular:* 20–40 mg. every 6 hours; optimal 25 mg. This level usually maintained for 10 days, after which it is gradually decreased, and discontinued after 10 mg. doses are reached.
	Long-acting vehicles: 80–160 mg. daily; optimal 80 mg. Dose may be much less in the newer, more potent preparations. May be used twice daily during initial stages of acute disease, taper after about 10th day.
Cortisone	*Topical:* 0.5 and 2.5 per cent. suspensions available commercially (*i.e.*, 5 and 25 mg./ml.); optimal 0.5 per cent. 15 mg./Gm. in ointment form.
	Subconjunctival: $\frac{1}{3}$, $\frac{1}{2}$ ml. 2.5 per cent. suspension; every 3 to 14 days as indicated by progress of disease.
	Systemic (oral or intramuscular): 300 mg. first day, 200 mg. next 2 days followed by 100 mg. for approximately 8 to 10 days, then taper off.
	Oral: may require up to 25 per cent. greater dosage, divided into four daily doses.
Hydrocortisone	*Local and intramuscular:* similar to cortisone.
	Oral: 100–150 mg. daily, initially.

Summary and Conclusions

Corticotropin and cortisone have proved to be valuable additions to the ophthalmic armamentarium. It must be emphasized that these are not last-minute agents, but efficient compounds whose maximum value is dependent upon their early use. The chief aim of all therapy is to cure an acute inflammatory or allergic (or traumatic) disease with a minimum of damage to the ocular tissue, at the same time preventing the development of a chronic process. The hormone selected must therefore be employed at an early stage in the disease. Experience has demonstrated that the final result depends upon the duration and severity of the disease process versus the potency, dosage, and length of treatment of the hormone. Hydrocortisone, the newest of the steroid hormones to be introduced to ophthalmology, still requires further research.

The intelligent use of these compounds requires recognition of the fact that corticotropin and cortisone are two different hormones, with two different modes of action. The fact that cortisone can be employed topically renders this the remedy of choice in the average case of superficial ocular disease. Deeper involvement may demand systemic therapy with either corticotropin or cortisone. Corticotropin employed as an intravenous drip over a period of 8 or more hours has so far proved the most effective systemic therapy. The introduction of the new high potency corticotropin gels has rendered ambulatory treatment possible in many patients who would formerly have required hospitalization. Combinations of local cortisone and systemic corticotropin (especially in a long-acting vehicle) or cortisone (especially in the oral form) can be employed profitably in the maintenance of chronic cases. All these preparations lend themselves to ambulatory treatment, with proper control. Complications rarely occur within the first 2 weeks of systemic treatment.

If the acute inflammatory process does not respond within a maximum of 48–72 hrs, one must then consider either increasing the dose or switching to the alternative hormone. It is unwise to risk damage to the eye by continuing a form of therapy which is not giving relief.

The presence of a positive culture or evidence of bacterial infection is an indication for the supplementary use of those antibiotics which will function in the presence of a normal or practically normal capillary permeability. Other supportive measures, such as the use of atropine and artificially induced fever, still have their place in treatment.

The fact that a chronic or subacute case will relapse upon the cessation of hormonal therapy is not a contraindication to its use. Such patients demand the full use of the ophthalmologist's skill in mapping out a maintenance programme which will combine the maximum safety with the maximum comfort or visual function.

The bulk of the corticotropin and all of the high potency corticotropin in long-acting vehicles used in this work was supplied by the Armour Research Laboratories through the courtesy

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OCULAR COMPLICATIONS OF MUMPS*

BY

D. P. NORTH

London

THE ocular complications of mumps are rare, the commonest being dacryoadenitis, which is usually bilateral and begins with sudden pain in the orbits, chemosis of the bulbar conjunctiva, and enlarged tense painful lacrimal glands. In its milder form it is called mumps conjunctivitis (Lippmann, 1943; Villard, Viallefont, and Teyssier, 1937; Galpine and Walkowski, 1952). Other complications are rare but the following have been described:

Keratitis (Danielson and Long, 1941; Nectoux, 1946; Roussel, 1946; Fields, 1947; Lippmann, 1943; Lundsgaard, 1923).—This begins from 2 to 11 days after the onset of the parotid swelling and shows conjunctival and circumcorneal hyperaemia, with interlacing linear opacities in the substantia propria, involving the whole area of the cornea. There is pain and lacrimation, with reduced vision. Roussel describes one case as having a visual acuity of 1/60. The condition is usually unilateral but may be bilateral. There is no evidence of uveitis, and complete resolution occurs in about one month, the cornea clearing from the periphery.

Scleritis (Berg, 1927: three cases).—There is pain with chemosis and scleral hyperaemia which resolves in about 15 days. Another case (Berg, 1931) showed a transient peripheral keratitis in addition to scleral inflammation.

Anterior Uveitis (Villard, Viallefont, and Teyssier, 1937; Ortega, 1932).—This occurs 2 to 3 weeks after the onset of mumps, no other cause being found. It responds readily to treatment with mydriatics. It is occasionally bilateral. One case (Roussel, 1946) occurred 8 days after the onset of mumps, and caused a rise of intra-ocular pressure to 35 mm. Hg, the visual acuity being reduced to 1/60. With mydriatics the intra-ocular pressure fell to 20 mm. Hg, and the vision improved to 6/6.

Choroiditis (Laje, Weskamp, and Boccalandro, 1939).—A patch of choroiditis, with surrounding retinal oedema reducing the visual acuity to 6/18 was noted, and 2 days later parotitis developed. The lesion increased with the parotid swelling and then underwent simultaneous resolution.

Papillitis and Optic Neuritis (Casserat, 1939; Swab, 1938; Powell and Dunlap, 1940; Young, 1933).—These manifestations are recorded as appearing from 2 to 4 weeks after the onset of mumps. There is usually gross impairment of vision with recovery during the following month. Casserat states that the prognosis is better with the complication developing early in the illness, because a later

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appearance is more likely to produce optic atrophy. One case of mumps encephalitis (Young, 1933) is reported as having no perception of light in either eye 3 weeks after the onset of the illness, and recovering normal visual acuity and fields one month later. Other cases are reported to have had permanently reduced visual acuity and fields. Powell and Dunlap describe a case of optic neuritis with paralysis of accommodation occurring one month after the onset of mumps which showed gradual complete recovery.

Ocular Nerve Palsies (Butler and Wilson, 1937: 2 cases).—The first case, a boy aged 9 years, developed parotitis and 3 weeks later had paralysis of accommodation, the pupil not reacting to light: there was also paralysis of the palate. Complete recovery followed. The second case, a boy aged 12 years, developed complete left oculomotor palsy one month after the onset of parotitis, followed 2 days later by an abducens palsy and palatal palsy. Improvement occurred slowly leaving a residual oculomotor weakness with dilated pupil and poor convergence. The authors state that the neurological complications can appear at any time from the period of maximum swelling of the parotid gland until 6 weeks afterwards.

Case Reports

(1) *Bilateral Sclerosing Keratitis and Anterior Uveitis following Mumps.*—During an epidemic of mumps in July, 1949, a girl aged 6 years developed mumps and was nursed at home by her mother aged 34. The illness ran a typical course and subsided without complications. Early in August, 1949, the mother became ill with a sore throat, headache, and pyrexia, followed in 2 days by tender swelling of the parotid and submaxillary glands. Swelling and tenderness slowly subsided over the next 3 weeks, but the headache persisted and the eyes became red and painful. On examination the general condition was good. Both upper eyelids were red and swollen. The upper bulbar conjunctivae on each eye showed intense hyperaemia from the limbus to the superior fornix, and multiple opalescent swellings, varying from 2–5 mm. in diameter. These swellings were very tender to pressure. The media were clear and the fundi normal. There was no increase in intra-ocular pressure. Ocular movements were full. The visual acuity was 6/9 in the right eye, and 6/12 in the left, unaided.

A general medical examination revealed no abnormality. Blood picture, cell counts, and sedimentation rate within normal limits. Kahn reaction negative. No oral, nasopharyngeal, or gynaecological sepsis. *X*-ray examination of the chest showed a calcified Ghon's focus in the right lower zone. Urine normal to routine examination and sterile when cultured.

The patient was treated with rest, atropinization, and hot bathings. Salicylates and antihistamine therapy had no appreciable effect. Short-wave diathermy aggravated the headache.

The condition slowly improved over the next 2 months, the gelatinous nodules slowly shrinking and leaving small chalky deposits. At the beginning of November, 1949, pain and redness reappeared. On examination there was conjunctival injection with a dusky ciliary flush. A fine deposit of cells and keratic precipitates was seen on the back of the cornea in the lower zone. A faint aqueous flare was noted. The fundi were normal and there was no increase in intra-ocular pressure.

Treatment with hot bathings and atropinization was resumed. One week later a tongue-shaped area of grey infiltration had appeared in the substantia propria of each cornea, extending from about 10 to 2 o'clock and invading the cornea for about 3 mm. towards the centre.

The lesions gradually regressed and in 3 months the eyes were white and comfortable and the vision unimpaired; 6 months later there had been no recurrence of symptoms.

(2) *Sixth Cranial Nerve (abducens) Paralysis following Mumps.*—A young man aged sixteen developed slight swelling of the parotid and submaxillary glands with pyrexia, on April 2, 1951. At the same time he had mild bronchitis. One week later there was high pyrexia, orchitis, severe headache, and signs of meningeal irritation. On the eleventh day, he complained of double vision. He was pyrexial for 23 days in all.

Examination on May 7, 1951, showed that his visual acuity was 6/5 in each eye, and that the only abnormality was a right external rectus muscle paralysis. He was seen every week and a slow but constant improvement was noted until June 22, 1951, when no abnormality was found and normal binocular vision was elicited.

Conclusion

Ocular lesions such as scleritis, keratitis, uveitis, and ocular palsies are often seen and fully investigated and no satisfactory cause found. The above cases and similar accounts found in the literature raise the possibility of virus infections, perhaps subclinical, as exciting or causative factors. A similar picture can be shown with herpes zoster ophthalmicus, in which the anterior uveitis and scleritis (when they occur) can be shown to be active long after the skin has completely healed.

Summary

A brief review is made of the reported cases of ocular complications of mumps. A case of sclerosing keratitis with anterior uveitis, and a case of abducens nerve palsy both following mumps are described.

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TISSUE THERAPY IN PARENCHYMATOUS XEROSIS*

BY

L. P. AGARWAL

Department of Ophthalmology, Medical College, Agra, U.P., India

PARENCHYMATOUS xerosis has been known for a very long time. Various therapeutic measures have been employed from time to time without any real success. The condition has been regarded as incurable, and Duke-Elder (1938) states that relief can be obtained only by oily drops.

Encouraged by the results of keratoplasty, I decided to try the operation of conjunctivoplasty in the so-called incurable condition of xerosis secondary to trachoma. Sorsby (1948) and Brown (1941) reported good results from the use of specially prepared amniotic membrane grafts in conjunctival burns, but as conjunctiva was at times not available it was decided to transplant amniotic membrane. As an experimental measure a 2-mm. piece of bulbar conjunctiva was removed, and a piece of specially prepared amniotic membrane of similar size was grafted in its place in two cases. The grafts did not take, and the membrane melted away, but surprisingly enough there was marked improvement in the xerotic condition in each case. It was therefore decided to apply the simple procedure of tissue therapy in xerosis.

In 1936 Filatov first introduced tissue therapy in retinitis pigmentosa by the implantation of pieces of placenta beneath the subconjunctiva, and reported a certain measure of success (Filatov and Verbitska, 1946).

Filatov (1937) also tried tissue therapy in trachomatous pannus. Implantations of preserved cadaver mucous membrane from the lip and conjunctiva led to gratifying results. Implantations of various tissues together with intramuscular injections of cod-liver oil were included among his therapeutic procedures, and he also used vegetable products such as aloe leaves. Saint-Martin (1950) describes the use of vegetable substances by subcutaneous injection and of skin as implant. Beneficial effects have also been reported by Olontzeva and Pokrovsky (1946). In the series here reported, 25 cases have been treated by this procedure and there has been marked improvement in all of them.

Methods and Material

Preservation of Placenta.—The placenta is received on a sterile towel and washed thoroughly with sterile normal saline to remove all blood clots. A small piece of about 1 cc. is cut out of a cotyledon, placed in penicillin in saline (2,000 to 5,000 units per ml.), and preserved in a refrigerator for 48 to 72 hours before use.

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Preparation of Patient.—Penicillin drops are instilled 2-hourly for 2 days before the operation. The lashes are cut and the eye cleaned on the morning of the operation. Care should be taken to exclude any discharge from the eye which may later lead to sepsis. Two per cent. anethane is used for local anaesthesia.

Technique of Grafting.—Small fragments of placenta of about 1 c. mm. are cut from the preserved piece. The bulbar conjunctiva is then cut and a pocket made and the small piece of placenta is placed in this pocket. There is no need to stitch the conjunctiva to keep the implant in position.

Post-operative Follow-up.—Procaine penicillin, 4 million units per day, is given intramuscularly for 5 days after operation. The bandage is opened the next morning and penicillin drops and liquid paraffin are instilled. There is no need for further bandaging as the conjunctiva heals within 24 hours.

Case Reports

For the purpose of treatment and review the cases were divided into three main groups:

(*a*) One or two dry patches were noticed in the angular portion of the conjunctiva just near the limbus (xerosis just beginning).

(*b*) The cornea was normal but the whole of the conjunctiva looked dry.

(*c*) The whole of the conjunctiva and cornea showed xerosis and vision was reduced to perception of light, or at best hand movements.

It must be stated at the outset that no cases of xerosis epithelialis were included because these can easily be treated by vitamin A injection in massive doses.

Group (*a*).—Thirteen cases were treated and the results obtained were remarkable. All appeared completely cured and no untoward reaction was observed. Most of the cases required grafting twice or thrice, and a few required as many as six grafts before the condition yielded to treatment.

Group (*b*).—Nine cases were treated and the results obtained were equally encouraging though it was a long time before good results were obtained. In a few cases as many as eight to ten grafts were given in each eye. In every case the xerosis started clearing from the fornix and the limbal region was the last to clear. The conjunctiva first regained its lustre, and the moistening of the conjunctiva by tears was the last stage in improvement.

Group (*c*).—Three cases were treated and the results obtained though encouraging were not so good as in the other groups. Considering that these patients were otherwise condemned to blindness, no other treatment being of any avail, the results obtained were a real improvement.

Case 1, male, aged 35, complained of gradual diminution of vision and a sensation of dryness in the eyes for the last 3 years. Follicles were present on the palpebral conjunctiva; the cornea was lustreless, dry, and practically opaque. Examination of the interior of the eye was impossible. Vision was reduced to hand movements only, both eyes being equally affected. After eighteen grafts vision in the right eye improved to 6/18 and in the left to 6/36. Dryness was still present over a limited area but the extent was less than before.

Case 2, male, aged 30, complained of gradual diminution of vision for the last 2 years. The conjunctiva and cornea in each eye were dry and lustreless. Vision in both eyes was reduced to hand movements. After twenty grafts, vision in the right eye was 6/36 and in the left 6/60. Dryness was completely absent.

Case 3, male, aged 37, had experienced gradual loss of vision for 2½ years. Treatment with oily drops had been given at various clinics without any improvement. The right eye was found to be the more affected. Vision in the left eye was 3/60 while in the right it was hand movements

only. After sixteen grafts vision in the right eye improved to 6/36 and in the left to 6/18. Dryness was still present in the right eye over a very limited area.

Pathology

A section taken from a biopsy before treatment (Fig. 1) shows stratified squamous epithelium on one side and loose connective tissue on the other. The epithelium as a whole is thickened and shows keratin deposits on the surface of its entire length except for one small area. The malpighian layer shows a well-marked stratum granulosum beneath the keratinized layer. The

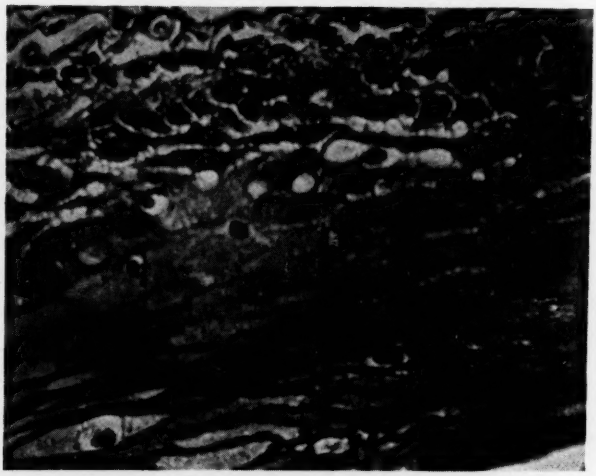

FIG. 1.—Section of conjunctiva biopsy before treatment. Haematoxylin and eosin. ×430.

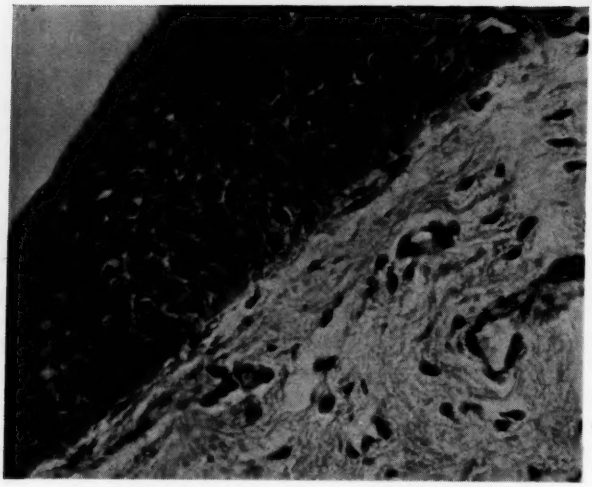

FIG. 2.—Section of conjunctiva biopsy after treatment. Haematoxylin and eosin. ×430.

cells are laden with blue-staining kerato-hyaline granules. The prickle cells show prominent intercellular bridges and some show mitosis and pyknosis. The individual prickle cells in some places show marked vacuolation just beneath the layer of cells containing kerato-hyaline granules. The cells of the basal layer are cuboidal and some show deposition of pigment, which is probably melanin. The subepithelial tissue shows prominence of blood vessels. There is marked round cell infiltration of lymphocytes and plasma cells. The distribution of inflammatory cells is at places perivascular and at others irregular.

After treatment the epithelium shows normal conjunctival histology with no evidence of formation of keratin. Goblet cells are not seen. In the subepithelial tissue a few lymphocytes are seen (Fig. 2).

Summary

Twenty-five cases of various grades of parenchymatous xerosis were treated successfully by subconjunctival implantations of placenta. The technique of preserving the placenta and the preparation of the patient for operation are described. The post-operative follow-up and final results in three types of case are reported. The first two were completely cured and in the third marked amelioration resulted.

The histological appearances of conjunctiva in parenchymatous xerosis before and after treatment are illustrated.

In this series, the condition known as parenchymatous xerosis, which has so far eluded treatment, was successfully treated by subconjunctival implantations of placenta. The mode of action of this tissue therapy is still uncertain but it is believed to be due to some kind of biogenic stimulator.

This work is published with the permission of Dr. H. N. Bhatt, Principal, and Dr. R. S. Varma, Professor of Ophthalmology, Medical College, Agra, U.P., India.

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TOPICAL USE OF TERRAMYCIN OINTMENT IN TRACHOMA*

BY

R. NACCACHE

Beirut, Lebanon

Methods.—Throughout this investigation we used ophthalmic tubes each containing $\frac{1}{8}$oz. of a 0.50 per cent. terramycin ointment.† The treatment was followed for 3 months in each case.

Material.—The patients were unselected; all the cases of trachoma who attended the Lebanese Red Cross Eye Clinic of Moussaitbeh were included, provided:

(*a*) they did not suffer from any other ophthalmic or debilitating disease;
(*b*) they attended the clinic regularly;
(*c*) they had not had other treatment for trachoma for at least 6 months;
(*d*) they used the ointment given to them regularly, twice a day.

Classification.—The patients were classified into four groups, according to MacCallan (1936). Only cases of Trachoma I, II, and III were treated. We did not follow MacCallan's sub-divisions of Trachoma I and II because:

(*i*) We found that cases of Trachoma I of the general lymphocytic type were difficult to diagnose clinically in the absence of laboratory facilities. Thus only the follicular type of Trachoma I, which is much more frequently met with in Lebanon, was considered.

(*ii*) We found that the sub-division of Trachoma II into (*a*) the follicular type, and (*b*) the papillary hypertrophic type was too theoretical. Most often our patients exhibit a mixture of these changes with predominance of one or the other. We tried to record the type of trachoma according to the follicles or papillary hypertrophy present.

(*iii*) Pannus was recorded as follows:
(+) —up to $\frac{1}{4}$ of the cornea,
(++) —more than $\frac{1}{4}$ of the cornea.
(+++) —pannus reaching pupil (patient's head illuminated by examination lamp).

Results

36 patients were treated without side-effects, or toxic or allergic reactions.

Trachoma I.—Six cases were treated, one male and five females, all under the age of 8. A clinical cure without scars was obtained in all of them.

Trachoma II.—Twenty-two cases were treated, fourteen males and eight females. This series comprised eleven cases of the follicular type including six cases of early Trachoma II, and eleven cases of mixed follicular and papillary hypertrophic type.

(*a*) A clinical cure was obtained in seven of the eleven follicular cases. Pannus was greatly reduced but did not disappear.

(*b*) A cure was obtained only in two of the eleven cases of mixed type with predominance of papillary hypertrophy (Figs 1*a* and *b* and 2*a* and *b* opposite). The rest showed great improvement. Scar formation in this group was more apparent.

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† Generously supplied by Chas. Pfizer and Co. Inc., New York.

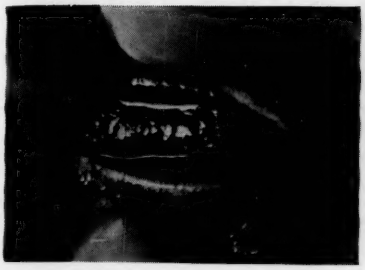

FIG. 1(*a*).—Case 35. Trachoma II with marked papillary hypertrophy. Right eye.

FIG. 1(*b*).—Same eye after 5 weeks terramycin therapy, showing flattening of papillary hypertrophy and scarring at upper edge of tarsus.

FIG. 2(*a*).—Case 34. Trachoma II with numerous well defined follicles. Right eye.

FIG. 2(*b*).—Same eye after 5 weeks terramycin therapy, showing decrease in number of follicles and fine criss-cross scars especially at temporal angle. The remaining follicles have lost their sharp edges and are flatter.

Trachoma III.—Eight cases were treated, all females. They showed some improvement, mainly subjective, but none was cured.

Comments

This investigation led to the following conclusions regarding terramycin:

(1) It is an effective drug against the secondary infection which plays such an important role in the evolution of the disease in the Middle East. This action is shown by the rapid subjective and objective improvement during the first week of therapy, especially in Trachoma II of the papillary type.

(2) It is a potent anti-trachomatous agent. This is shown by the disappearance of the follicles in cases of Trachoma I and early Trachoma II where there was a minimum of secondary infection.

The effect of terramycin was found to vary according to several factors:

(*a*) *Duration of Disease.*—The improvement was greater in recent cases.

(*b*) *Grade of Trachoma.*—Trachoma I and early Trachoma II were more sensitive, Trachoma III was more resistant.

(*c*) *Type of Trachoma.*—The response of the papillary hypertrophy was better at the beginning of the treatment, but from the 4th to 6th week a stationary condition

was reached, whereas the follicles which responded slowly at first continued to decrease.

(*d*) *Degree of Involvement of Tarsus.*—As one might expect, cases with an infected, thick, and distorted tarsus responded poorly to terramycin.

(*e*) *Age of Patient.*—Younger patients responded better than older ones, other things being equal. Up to 20 years of age the response was generally good.

Our results, though not so brilliant as those of Mitsui and others (1951) seem to be better than those obtained by Siniscal (1952). We believe that the classification used by Mitsui (1952) explains why this author obtained clinical cures in such a short period as 2 or 3 weeks. Cases which this author describes as acute trachoma belong by MacCallan's classification to the general lymphocytic type of Trachoma I. These cases represent the earliest clinical stage of trachomatous infection and are rarely met with in Middle East eye clinics. Patients in Lebanon report to clinics only when lacrimation, photophobia, sensation of foreign body, or discharge become troublesome. All these symptoms are largely due to secondary infection and indicate a certain duration of evolution in the trachoma.

We agree with Siniscal (1952) when he states that trachoma and its response to therapy vary to a great extent according to the country, climate, race, and habits of patients. This might be the reason why terramycin acted only on secondary infection in his patients.

In our cases, the best results were obtained in cases of Trachoma I which were found during a routine examination of symptom-free and apparently healthy children, in whom secondary infection could be practically eliminated.

Conclusion

Terramycin is a very valuable drug for the treatment of trachoma. It has the advantage over sulfonamides in quicker action, and the absense of toxicity permits longer treatment, especially in cases of children, pregnant women, and debilitated patients.

Mechanical, caustic, or surgical treatments may still be indicated in stubborn cases or in those with deep involvement of the tarsus, but only after an extensive trial of terramycin.

Summary

Thirty-six cases of trachoma were treated during a period of 3 months by local application of a 0.50 per cent. terramycin ointment. Six cases of Trachoma I were cured; seven cases of early Trachoma II were cured; fifteen cases of Trachoma II were greatly improved; eight cases of Trachoma III were moderately improved.

Terramycin was found to be a potent drug against secondary infection and trachomatous lesions.

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CASE NOTES

MALIGNANT MELANOMA OCCURRING AFTER EVISCERATION*

BY

B. A. BEMBRIDGE AND J. McMILLAN

From the Nuffield Laboratory of Ophthalmology and Oxford Eye Hospital, Oxford

WE report a case in which a malignant melanoma was found in the orbit 16 years after evisceration of the eye. The report seems justified as an illustration of the peculiarities of orbital swellings in general and because of the rarity of such a case.

Clinical History

1931: The patient (male, aged 53) attended hospital complaining of pain in the left eye. The eye had been practically useless since a cataract had developed after it had been struck by a hockey ball in his youth. The right eye was normal. On examination the left eye showed only poor projection of light, an anterior chamber occupied by the lens, and what appeared to be exudate lying behind this in the vitreous. No note was made of the intra-ocular tension. Kaolin poultices relieved the pain, and the patient was advised that the eye should be enucleated within a month or two; but he did not attend again for 5 years.

1936: He suffered another acute attack of pain in the left eye. On examination, gross oedema of the cornea and chemosis hid the details of the anterior chamber; evisceration was performed.

The operation note states that evisceration was difficult because of much fibrosis and profuse bleeding; it included " removal of the sclerotic, except for a cuff round the optic nerve ". The socket healed satisfactorily and the patient was discharged.

1943: He attended again with the left socket swollen and inflamed and examination revealed " conjunctiva of socket swollen and with a dark central patch, like uveal pigment ". Heat again relieved the pain and lateral tarsorrhaphy was performed for ectropion.

1952: In January the artificial eye fell out and broke and 3 months later he came to hospital for a new one. Examination showed a large mass in the left orbit which was causing some bulging of both lids, and greatly reducing the cavity of the socket so that a normal-sized prosthesis could no longer be retained. He had noticed a progressive swelling in the orbit since the glass eye had fallen out. Inspection of the upper and lower fornices revealed a dark mass beneath the conjunctiva. On palpation this was firm and appeared to fill the orbital opening almost completely. The dark mass was thought to be neoplastic. No suspicious cervical glands were palpable and a general medical history and examination revealed no evidence of a primary growth; a prostatectomy had been carried out in January, 1950 and the sections pronounced benign. *X* ray of the chest did reveal lesions at the right base compatible with early metastases, though inflammation could not be ruled out.

Exenteration of the left orbit was performed and the clinical findings confirmed. The

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mass extended back to the apex of the orbit and was attached firmly to the roof and lateral wall. It was particularly difficult to separate it from the roof, and when this had been achieved as completely as possible, the orbital plate of the frontal bone was seen to be considerably eroded. It was thought that intracranial extension must inevitably have occurred. The orbit began to heal remarkably well and 3 weeks later was packed with radium needles in Perspex beads to give a dose at the surface of the orbit of 6,000 r in 4 days. A rather profuse discharge has now cleared up, and epithelium completely lines the orbit.

The right eye is normal for his age (74 years), with uncorrected visual acuity of 6/9 and full peripheral field.

Pathology

Macroscopic.—No scleral remains could be recognized in the orbital contents, which contained numerous pigmented and non-pigmented nodules varying in size up to 2.5 cm. diameter. Some necrosis had occurred in the largest nodule. The nodules were apparently not muscular in nature, nor fibrous, for fibrous tissue separated the individual nodules. It could not be said, however, that there was an encapsulated tumour present in the orbital contents. The tissue from which the nodules originated could not be identified. Blocks were taken from different parts of the growth to try to discover its origin.

Microscopic.—The predominant cell of the nodules was spindle-shaped, with pale cytoplasm but with the nucleus staining more densely (Fig. 1). There was considerable variation in the cell type. The amount of pigment also varied; it was found both intra- and extra-cellularly, but large areas were completely without pigment. The cells were densely packed, except at the edge of some of the nodules where they were separated by collagen fibres, as shown by the van Gieson stain. In some areas the cells were arranged in whorls. Occasional multinucleate forms (Fig. 3) were seen. Mitotic figures were infrequent; one is seen in Fig. 1. In spite of the extent of the tumour, necrosis was slight. The reticulin content varied; a moderately reticulated area is shown in Fig. 2. The histological picture was that of a scantily pigmented malignant melanoma of mixed cell type. The optic nerve could not be identified, so that it was not possible to say if there was any likelihood of extension retro-orbitally.

Discussion

The histological sections do not show from what structure the neoplasm originated, so discussion of the case can only summarize its possible origins. If the possibility is discounted that the tumour was a secondary deposit from a distant primary, the other possibilities to be considered are that it was a primary orbital melanoma, or had extended into the orbit from uveal cells remaining after the evisceration.

Malignant melanomata can originate in the orbit, but they are rare (Parsons, 1905; Offret, 1951). There were none in the series of 31 orbital tumours reported by Dandy (1941), and one of a series of 251 primary orbital tumours described by Reese (1951a) is described as a malignant schwannoma. Jackson (1951) says that melanoma can be found within the muscle cone, and he includes the condition in his tabular analysis of the pathology of 125 cases of orbital tumours. Rottino and Kelly (1942) reported one case of

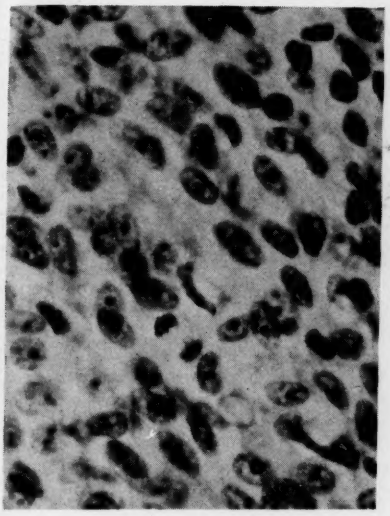

FIG. 1.—Predominant cell type. Mitotic figure in centre of field. Haematoxylin and eosin. × 680

FIG. 2.—Reticulin. Gomori. × 580

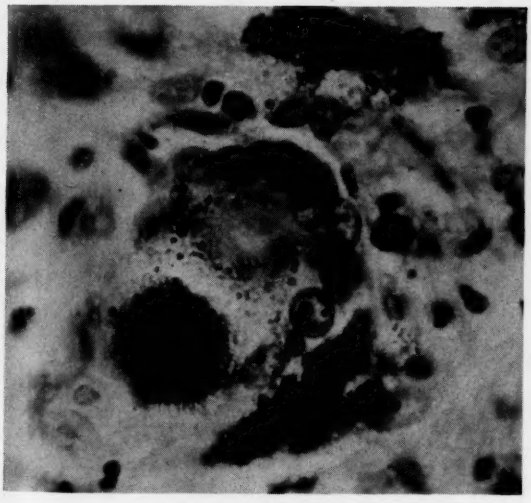

FIG. 3.—Multinucleate cell at edge of a necrotic area. Haematoxylin and eosin. × 680.

primary orbital melanoma, and after an extensive review of the literature as far back as 1838, they summarized eleven cases, but histological details were not complete in all of them. Foster (1944) reported a case of encapsulated orbital melanoma, but there was some doubt as to whether it was a malignant growth. Single cases have also been reported by Offret (1951) and Bonnet (1951).

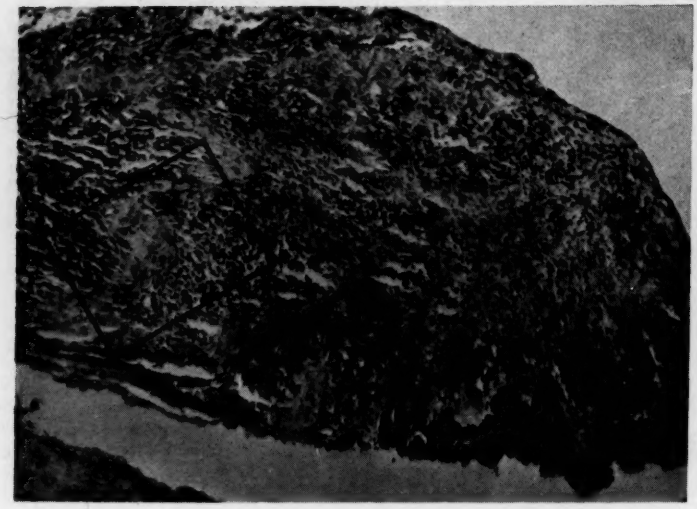

FIG. 4.—Tumour cells to left and centre of field, approaching epithelial surface below and to the right. Haematoxylin and eosin. × 90.

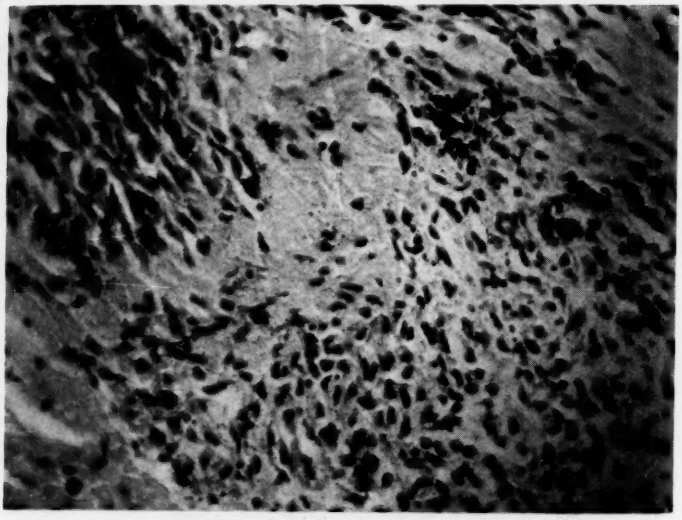

FIG. 5.—Higher-power view of the inset of Fig. 4. Haematoxylin and eosin. × 380.

In our case, section through the lid (Figs 4 and 5) showed the tumour infiltrating close to the epithelium, but no evidence of its origin from a conjunctival naevus could be found. Similar proximity of part of the tumour to nerve fibres (Fig. 6, opposite) is also insufficient evidence that the tumour originated from Schwann cells.

It seems more likely that the tumour arose from uveal cells left behind at the time of operation. Speculation whether these cells were already

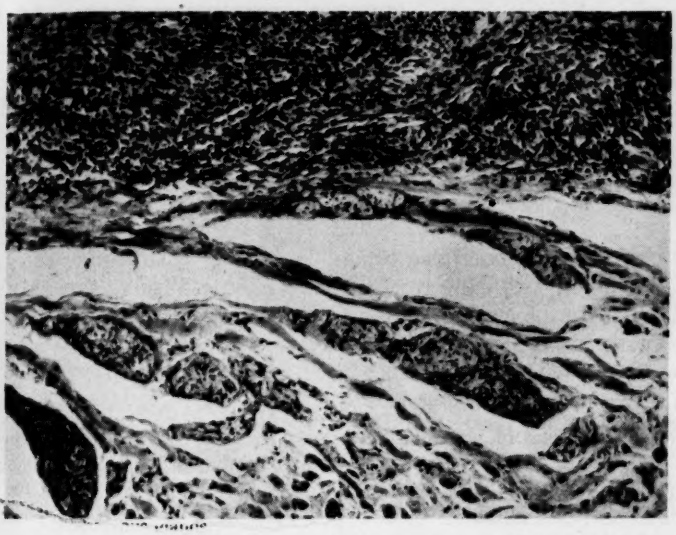

FIG. 6.—Infiltration of the tumour close to nerve fibres. Haematoxylin and eosin. × 90.

neoplastic, about the part played by the original injury and subsequent inflammation, and about the possibility of a benign lesion becoming malignant, is profitless. The most likely explanation may be that there was already a neoplasm present at the time of operation in 1936, but it still remains an interesting case as an example of extensive local recurrence. Terry and Johns (1935) observed that although malignant cells are frequently left in the orbit after enucleation for a malignant melanoma, orbital recurrence is seldom seen and this opinion seems to be that generally held. Davenport (1927) examined the records of 35 cases of sarcoma of the uveal tract and could find no evidence of orbital recurrence in the 22 cases he traced. Newton (1938) reported one case, and Reese (1951b) has seen eight such cases. Cairns (1922) reported metastasis to the scapula 18 years after enucleation of the eye for malignant melanoma, and clinical examination indicated the probability of local recurrence also. Further case reports may help to elucidate why the orbit seems to be an unfavourable site for the continued growth of malignant cells after the removal of a uveal tumour.

We wish to thank Mr. Victor Purvis, under whose care the patient has been since 1952, for permission to use the details of the case history.

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Brit. J. Ophthal. (1953) **37**, 114.

EXCISION OF A LARGE ORBITAL DERMOID CYST*

BY

MILROY PAUL

University of Ceylon

EVERY operation for the excision of an orbital dermoid cyst extending deeply into the orbit is fraught with danger of operative trauma to the contents of the orbit. The results of such operations are worthy of record as they assist a correct assessment of the operative risk.

Case Report

T. J., a male Ceylon Tamil aged 15, was admitted to the General Hospital, Colombo, on April 29, 1952, on account of a tumour growing within the right orbit. The tumour had been noted when he was one year old and had been growing steadily larger, the sight of the right eye having been impaired for the last 7 years.

Examination.—A soft, fluctuant, oval mass bulged forwards under the right upper eyelid and occupied the space between the upper orbital rim and the eyeball (Fig. 1). The eyeball was pushed downwards $\frac{3}{4}''$ below the level of the left eyeball, and the right orbit was wider than the left. There was no proptosis. The movements of the right eyeball were not impaired and there was no squint. On eversion of the upper eyelid, an oval mass could be seen bulging the upper conjunctival fornix. The tumour was not adherent to the eyelid or conjunctiva. No pulsations were detected on palpation.

Diagnosis.—The long duration of the tumour classed it as a non-malignant growth and its round, smooth shape and fluctuant consistency suggested that it might be an orbital dermoid. The absence of pulsation in the tumour, and the fact that a radiograph showed no abnormal aperture between the orbit and cranial cavity suggested that the cyst was not a meningocoele. The widening of the right orbit is seen in Fig. 2.

The steady enlargement of the tumour, the facial distortion produced by displacement of the eyeball downwards, and the deterioration in the sight of the right eye made removal of the tumour desirable. Its position made damage to the levator palpebrae

FIG. 1.—Before operation.

FIG. 2.—*X* ray showing distortion of orbital cavity.

* Received for publication July 22, 1952.

FIG. 3.—Photomicrograph of cyst wall showing skin and sebaceous glands.

FIG. 4.—After operation.

superioris an operative risk and as this injury might prevent use of the right eye besides being very unsightly, careful consideration was made of the possible routes of access. The approach through the upper fornix of the conjunctiva was selected.

Operation.—Under general intratracheal anaesthesia, an incision was made through the conjunctival fornix. The tumour was found to be covered by a layer of orbital fat and on clearing this a white wall was exposed. The cyst extended deeply into the orbit. It was opened during the dissection, and cheesy debris with fine white downy hairs extruded from its lumen, but this partial emptying of the cyst greatly facilitated the dissection. A probe introduced into its lumen showed it to be sausage-shaped and to extend 40 mm. back to the apex of the orbit. The cyst wall was carefully drawn forwards and it was eventually dissected right out of its bed (Fig. 3). There was no appreciable bleeding. No sutures were placed in the wound in the conjunctival fornix.

Results.—The next day the upper eyelid was swollen, and could not be raised; 4 days later the swelling was less and the lid could be raised sufficiently to open the eye. The movements of the eyeball were unimpaired. The patient made a good recovery (Fig. 4), and when he left hospital on May 16, 1952, could open the right eye readily, but he could not retract the upper eyelid while looking upwards, and when he closed the eye the lower lid moved upwards to the upper lid. He was however well satisfied to be rid of the cyst, and to be able to use the eye much more efficiently than before.

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Brit. J. Ophthal. (1953) 37, 116.

UNUSUAL CASE OF INTRA-OCULAR FOREIGN BODY*

BY

G. M. BARLING

Peterborough

IT may not be generally realized that the magnetic properties of certain types of steel differ considerably from those of ordinary carbon steel and that these magnetic properties may alter under certain circumstances.

Case Report

A patient who recently came under my care had been struck in the right eye by a foreign body whilst hammering a piece of steel with hammer and cold chisel. A diagnosis of intra-ocular foreign body was made, there being a small entrance wound in the centre of the cornea and an opaque lens. This diagnosis was confirmed by *x* ray. The foreign body, measuring about $3\frac{1}{2} \times 1 \times 1$ mm. was located in the posterior segment of the globe. Operation was performed on the same day (that following the injury) and an attempt was made to remove the foreign body by the posterior route. This attempt was unsuccessful, much to my surprise, as the foreign body was a large one and should have come out easily. I had originally been told both by the patient, and by his employer, that the foreign body had come from the metal which he was working and not from his chisel or hammer, but I was inclined to view this with some scepticism as it is generally found that the foreign body is provided by the workman's tool rather than by the metal being worked.

After this failure to remove the foreign body I decided to investigate the matter further. Unfortunately the eye became infected and had to be removed about a week later. The foreign body was retrieved from the posterior segment where it was lying almost up against the disk, with one end in fairly close proximity to the operation wound.

The foreign body was sent to the laboratory at the factory where the patient worked, and was found to be a piece of austenitic steel of the type on which he was working at the time of the accident. It did not come from the hammer or chisel. Austenitic steels, of which stainless steel is an example, are non-magnetic in the normal state, but acquire slight magnetic properties on being cold worked—chipping with a chisel is an example of such cold working. These steels are used in industry for their heat-, scaling-, and rust-resisting properties. Fig. 1 shows the fragment of austenitic steel actually removed from this patient's eye; Fig. 2 shows fragments obtained by chipping with hammer and chisel.

Investigation

The magnetic properties of this piece of steel were compared with those of a piece of ordinary carbon steel of similar size.

Specimens

(*i*) Chipping removed from the patient's eye in hospital.
(*ii*) Chipping taken from a piece of spring steel.

* Received for publication October 22, 1952.

FIG. 1.—Steel fragment removed from patient's eye. ×10.

FIG. 2.—Steel fragments obtained by chipping with hammer and chisel. ×3½.

Method of Comparison.—The chipping was suspended by a light thread from one side of a balance beam. A coil with a soft iron pole piece was interposed between the chipping and the balance pan. Weights were added to the other balance pan and the air gap between the chipping and the soft iron pole piece adjusted to a fixed distance which was kept constant during the experiment. The current to the coil was switched on and increased until the attraction between the chipping and the iron pole piece was sufficient to overcome the " off balance " caused by the weights on the other pan. The experiment was repeated, more weights being added to the balance pan and the current being increased until attraction (indicated by the swing-over of the balance) took place. The experiment was repeated until a stage was reached when further increases in current did not result in greater weights being overcome by the magnetic attraction. It was then assumed that the chipping was magnetically saturated. The current and the maximum attraction in milligrammes was recorded.

Points investigated	Type of Steel Chipping	
	Stainless	Carbon
Mass of chipping	0·023 g.	0·023 g.
Weight required to " off balance " weight of chipping plus thread to extreme left	0·070 g.	0·070 g.
Maximum weight overcome by magnetic attraction	0·159 g.	2·75 g.
Air gap between pole piece and chipping	0·081"	0·081"
Current	0·38 amps	0·38 amps
No. of turns on coil	4730	4730

The experiment was now repeated with the carbon steel chipping under identical conditions, using the same air gap between pole piece and chipping, and the same coil and current. It was ascertained in the same way as before that the current was sufficiently high to cause magnetic saturation of the chipping.

Observations.—Since both specimens were of equal mass and similar shape, and were both tested at an equal distance from the same coil carrying the same current, under conditions whereby both specimens were magnetically saturated, a direct comparison (in milligrammes) of their magnetic properties was possible. Moreover the general conditions of the experiment were similar to those which would prevail in the extraction of a metallic splinter from the eye in an Ophthalmic Department.

Type of Steel Chipping	Maximum Attraction
Stainless	0·159 − 0·070 = 0·089 g.
Carbon	2·75 − 0·070 = 2·68 g.

$$\text{Ratio of carbon steel to stainless steel } \frac{2{\cdot}68}{0{\cdot}089} = 30{\cdot}1.$$

It would thus appear that, other factors being equal, to remove a piece of stainless steel embedded in the cornea or within the globe might require mechanical force thirty times greater than that required for removal of a fragment of carbon steel identical in size.

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LOSS OF SIGHT FOLLOWING SNAKE BITE*

BY

R. C. DAVENPORT AND F. H. BUDDEN

London, and the Colonial Medical Service, Nigeria

Loss of sight following haemorrhage is a long established clinical entity, but its pathology and the causation of the optic atrophy are still uncertain. The following case, to which we have been able to find no parallel in the literature, shows an unusual cause of bleeding leading to loss of sight.

Case Report

Notes of Original Lesion.†—A European male, aged 51, was admitted to hospital at 7 p.m. on *February 11, 1952*, within half an hour of being bitten by a viperine snake on the dorsum of the left foot (specimen identified as *Echis carinatus*). He was treated immediately by tourniquet and incisions of the bitten area under pentothal; 10 ml. antivenine were injected locally and 10 ml. intramuscularly.

February 12, his general condition was good, but the incisions started oozing blood and continued to do so, despite styptics and pressure dressings.

February 13, the systolic blood pressure fell to 85 mm. Hg, and the erythrocytes to 2.5 million, necessitating immediate blood transfusion (450 ml.) with marked benefit.

February 14 and *15*, slight oozing only of wounds and mucous membranes of mouth, but extensive extravasation of blood into muscles of thigh and buttocks at sites of penicillin injections and application of tourniquet. The oozing from the incisions was well controlled and there were no local or general signs of sepsis and no leucocytosis. On these two days the haemoglobin figures were 60 per cent. and 65 per cent.

February 17, general condition very poor with the blood pressure 85 systolic. For the first time he complained of lower field blindness of the right eye. A second blood transfusion (500 ml.) started at 12 noon raised the systolic blood pressure to 120, and his general condition improved.

February 18, no change occurred in the vision of the right eye.

February 19, In the morning he complained of " blind spots " in the temporal field of the left eye.

February 20, both pupils reacted to light but the left pupil was a little larger than the right. No perception of light was present in the lower right visual field; there were no obvious changes in the disks. The haemoglobin was 65 per cent. and a further blood transfusion of 500 ml. was given.

February 21, the left eye was worse subjectively and the pupil a little larger than before but still reacting to light though dilating almost at once.

February 22, there was no perception of light in the left eye and the pupil response was negligible.

February 23, haemoglobin 75–80 per cent. and the blood pressure 120 systolic; the patient's general condition was excellent.

* Received for publication October 13, 1952.

† Kindly supplied by Dr. D. W. McLaren, Medical Officer in Charge, Kaduma Area, Nigeria.

Ophthalmic Findings (*F.H.B.*). *February 28, 1952*

Right eye—6/6 with correction. Loss of lower half of visual field; the patient describes the line of demarcation as quite sharp and as passing through the middle of any object at which he looks (*e.g.*, print in a book); pupil reacts normally to light and accommodation; fundus—disk edges blurred both above and below, all veins distended, especially on and near the disk; retinal oedema around disk; no haemorrhages or exudates seen.

Left eye—no perception of light; pupil—no direct reaction to light but consensual reaction normal; fundus—disk swollen and edges blurred, especially above and below; veins distended; small haemorrhages at and near the disk margin, retinal oedema making the fovea stand out red; pinpoint exudates to the temporal side of the disk and over the macular region.

Ophthalmic Findings (*R.C.D.*). *April 7, 1952*

Right eye—6/5 with correction; sharp horizontal demarcation of visual field with all the lower half lost; direct pupil reactions brisk; media clear; optic disk clear cut and pale generally but all blood vessels quite normal in appearance.

Left eye—bare perception of light in all directions, best in upper temporal quadrant; no direct pupil reaction; sharply defined, very pale disk with arterial branching grossly attenuated.

Both fundi otherwise normal.

Discussion

Echis carinatus is a true viper of particularly malignant type found in hot desert surroundings, *e.g.*, Kaduna. Recent papers by French medical officers (Giboin, 1951; Salou, 1951) suggest that *Echis carinatus* in Africa is larger and even more deadly than the Indian variety (Purohit, 1944) and that its bite is almost invariably fatal. Prompt sustained efficient treatment saved this patient's life, and this fact, with the severity of the bite, provided the unique clinical picture. Echis venom contains in addition to anticoagulants and haemolysins much haemorrhagin, and death after a bite is usually due to multiple haemorrhages and/or possibly depression of the vaso-motor centre. It may occur from 1 to 5 or more days after the bite. The only neurotoxic effect is on the vaso-motor centre. It seems quite unequivocal that the loss of sight in this case was related to the actual bite, and therefore to the bleeding which the venom caused. The only other possible element was that the patient was given four tablets each of 0.20 g. " Nivaquine " brand chloroquin sulphate, as in the course of blood examination two doubtful malaria parasites were found. We can find no evidence of this drug producing amblyopia even when given in very much larger dosage, and we cannot think it played any part in the sequence of events.

The case history follows the usual pattern, for the amblyopia did not immediately follow the repeated bleeding, one eye losing sight on the sixth day after the bite, and the other on the eighth day. At no stage was a very low haemoglobin level found, though low systolic blood pressure readings preceded the blindness. Further, total blindness did not result, the retained field being as usual the upper. Even in the left eye, such perception of light as remained was more definite in the upper field.

The interpretation seems to us to be that of retinal arterial spasm affecting first the right eye, and presumably lasting long enough only in the upper branches of the artery for complete death of the ganglion cells. The passing of the spasm allowed refill to normal appearance of the whole arterial tree, although the general pallor of the disk must mean some atrophy over all the inner retina. The spasm in the left eye was of such intensity as to produce total optic atrophy and permanent narrowing of the vessel. The appearance of oedema subsequent to the loss of sight has been frequently described and may be explained by damage to the capillary endothelium due either to the actual lowered blood supply, or as in capillaries elsewhere to the direct effect of the snake venom. The whole picture fits in well with the explanations of the course of events given by Wolff (1935) but provides no clearer reason for the selective severity of damage to the upper retina than his suggested explanation of gravity. Certainly this patient was nursed for the most part with the head partly raised.

The literature consulted (Lewin and Guillery, 1905; Phisalix, 1922) contains some generalizations on loss of sight following snake bite and amaurosis before death is mentioned, but as stated above we have been unable to trace any report of a case similar to this one. The only other remotely related case was that of a man admitted to Moorfields Eye Hospital with amblyopia which he attributed to the effects of a snake bite. In this case there was no proof of the viperine nature of the snake, no history of haemorrhage, and no pathological findings. Diagnosis of an ocular psycho-neurosis was borne out by the complete recovery which resulted, and the history did not even suggest that the psycho-neurosis was based on any physical lesion due to the snake bite, the effects of which had passed quickly before the case came under observation.

We wish to thank Dr. S. L. A. Manuwa, Director of Medical Services, Nigeria, for permission to publish the case, and Dr. C. J. Hackett, Director of the Wellcome Museum of Medical Science, and Dr. R. B. Hawes of the Colonial Office for help and advice about snake bite and the effects of venom.

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Brit. J. Ophthai. (1953) **37**, 122.

CRATER-LIKE HOLE IN THE OPTIC DISC*

BY

REDMOND SMITH

London

CASES showing a crater-like hole in the optic disc accompanied by a field defect have been only infrequently described in the literature. A series was reported by Rosen (1948). The usual features mentioned are well typified in the case reported below.

Case Report

A man aged 44, a property manager, had noticed several years before, when the right eye was affected by a stye, that his left vision was defective. He thought that his left eye had always been weaker than the right and he had worn glasses since childhood. He had never had pain or seen halos and there was no family history of eye defect. His general health was good.

Examination.—The anterior segments were normal and the media clear. The globes were of equal size.

Right eye showed an inferior crescent to the optic disc. Vision was 6/18 $\bar{c}\,\frac{-2.00}{+3.00} \times 120$. There was no field defect.

Left eye showed a deep narrow crater in the lower part of the disc into which the retinal vessels dipped. In the depths of the crater the vessels could be seen describing a loop downward as though lining a cystic space.

The lower half of the fundus was considerably paler than the upper. The choroidal pattern was clearly visible as in an albino, whereas the upper fundus was normally coloured (Fig. 1). Vision 6/36 pt. $\bar{c}\,\frac{-0.50}{+2.50} \times 50$. Perimetric examination showed an upper temporal quadrantic defect which was enlarged to loss of the complete upper half of the field on the screen. A curious feature of the field loss was the fact that the quadrantic

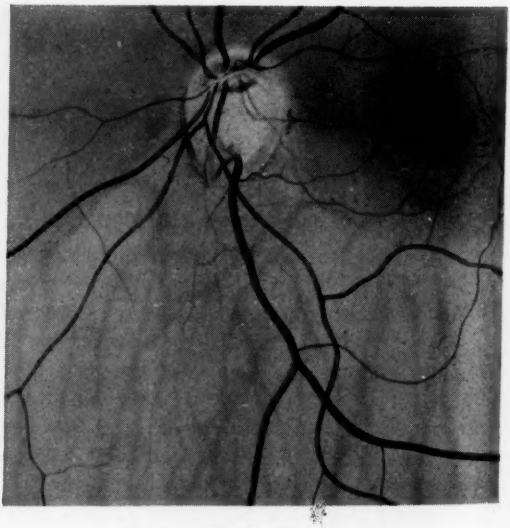

FIG. 1.—Drawing of left fundus

* Received for publication September 15, 1952

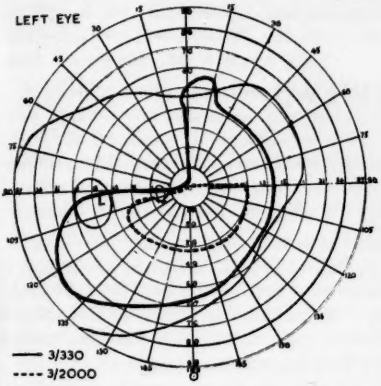

FIG. 2.—Fields in case of crater-like hole in the optic disc. The Bjerrum-screen field has been transposed on to the perimeter chart to save space.

defect had its apex at the fovea and not at the disc as might be expected (Fig. 2).

The ocular tension remained within normal limits during a 48-hr. in-patient check up.

Discussion

Clinically such cases are usually found accidentally at routine examination. The large field defect is a relatively constant feature although smaller scotomata may occur (Duke-Elder, 1941) and there may be macular changes. A case described by Rosen (1948) had a completely albinotic fundus and an atrophic iris.

The differential diagnosis from glaucoma is made on the localized nature of the pit which is usually in the lower temporal quadrant of the disc and is surprisingly small in view of the large field defect. In the case described above, it may be that the size of the field defect was partly attributable to the defective pigmentation of the lower half of the fundus. This area could be regarded as a minimal choroidal coloboma.

According to Duke-Elder the pathology consists of an out-pouching of the secondary optic vesicle, the cyst lining containing retinal elements. Mann (1937) points out that the last part of the foetal fissure to close and to acquire full pigmentation is a small area at the lower margin of the disc. She describes two types of ectasia in this region; an intra-neural type which probably corresponds to the crater-like pit, and an extra-neural in which the ectasia is outside the disc edge.

Whereas the intra-neural type usually remains as a small pit, the extra-neural may enlarge to form a cyst presenting the well-known combination of microphthalmia with cyst. There is a case, however, described by Greear (1930) in which the optic nerve itself was much distended by a large cyst.

Summary

A case is described of a crater-like pit in the optic disc associated with a large field defect. It was thought to be a congenital anomaly.

My thanks are due to Dr. Margaret Falconer and Mr. F. A. Williamson-Noble for their kind permission to examine this case and to use the facts here reported.

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Brit. J. Ophthal. (1953), **37**, 124.

BOOK REVIEWS

Le Trachome. Historique, Clinique, Recherches Expérimentales, Etiologie, Thérapeutique, Prophylaxie. (Trachoma. History, Clinical Results, Experimental Work, Aetiology, Therapy, and Prevention.) By ROGER NATAF. 1952. Masson, Paris. Pp. 416, 46 figs, 16 col. pl.

This comprehensive volume on trachoma is embellished by coloured plates, fifteen of which appeared in the "Atlas de biomicroscopie de l'oeil" published by the Société française d'Ophtalmologie in 1934, as the result of the painstaking labour of Cuénod and the present author. Their display at the Ophthalmological Congress in that year created a sensation, which was shared by the reviewer who was present.

The author has had an enormous experience of trachoma in Tunisia; he was at first assistant to Cuénod, the grand old man of trachomatology, and now he follows in Cuénod's footsteps. Cuénod and Nataf opened the eyes of trachomatologists to the importance of slit-lamp examination in all cases of conjunctival inflammation, with special reference to its absolute necessity in the precicatricial stages of trachoma.

Nataf is a member of the Expert Committee on Trachoma set up at Geneva by the World Health Organization, and he now provides our first information regarding some of this committee's activities. MacCallan's description of the four stages of trachoma have been adopted for administrative purposes, but certain symbols are added for clinical and scientific appreciation of the varieties of the disease; these the author describes, but they appear to him to be somewhat complicated.

Nataf's operation of combined excision of tarsus and conjunctiva for trichiasis-entropion, which differs from that described by Heisrath and Kuhnt, and later by MacCallan, has been performed with success on about 40,000 persons. It comprises an incision along the free border of the lid, as first described by Anagnostaki, and, after a skin incision, the removal of some tissue from the dorsal surface of the tarsus as in Streatfield's operation.

The treatment of the second stage of trachoma by mechanical therapy, which Nataf calls xysis, has given immediate and satisfactory results in the great majority of cases during the last 25 years. Now that sulphonamides and antibiotics are available they may be used with advantage, though they have no specific action on the trachoma virus, and xysis is commonly employed as the main line of treatment in Tunis.

This attitude to the treatment of trachoma, which to the reviewer appears to be sound, is entirely contrary to that appearing in the Report issued in 1952 by the Expert Committee at Geneva mentioned above. In this report in French and English (*Revue Internationale du Trachome*, **29**, 275, 1952) it is stated that mechanical treatment is unjustified except in a limited number of cases, complete reliance being placed on ingestion of sulphonamides and local application of antibiotics.

The author devotes eighty pages to the chapter on aetiology, pathology, and experimental research. He concludes that trachoma begins as an epitheliosis, but that the process is not limited to the epithelium, as it extends to the subepithelial tissue and, in all long-standing cases, to the tarsus. The aetiological agent appears to be a parasitic corpuscular virus which he calls *Prowazekia trachomatis*. As the first report on the subject was published in 1907 under the combined authorship of Halberstaedter and Prowazek, a discovery which initiated all virus research, it seems that the appellation *Halberstaedter-Prowazek Körperchen*, abbreviated to H.P.K., is only doing justice to the

duality of the discovery. (Halberstaedter, L., and Prowazek, S. von (1907). *Arb. GesundhAmt., Berl.*, **26**, 44, and *Berl. klin. Wschr.*, **47**, 661. Prowazek, S. von (1907). *Arch. Protistenk.*, **10**, 336 and 358.)

A chapter on the physiopathology of the trachomatous eye has been contributed by Jean Sédan, who has made this subject his own. He remarks that few authors have noted the frequency of increased tension of the glaucomatous eye, among them Cuénod, Nataf, and Bietti. He has forgotten that MacCallan (1921) (Egyptian Ophthalmic Hospitals Report for 1921) found that out of 127,223 new patients examined, 1.77 per cent. exhibited signs of primary glaucoma, and 1.34 per cent. absolute glaucoma.

The difficult question of trachoma prophylaxis in the family, at school, and at work is discussed. " Dès sa naissance, a dit MacCallan, l'enfant de mère trachomateuse est fatalement destiné à contracter la maladie ". However, according to the report of the Committee of Experts of W.H.O. (*Rev. int. Trachome*, **29**, 275, § 3.1, 1952), "trachoma is to be considered only slightly contagious ".

At school adequate prophylaxis may be attained if meticulous precautions are taken; trachoma contracted in the Army, or while at work in a factory, or claimed to be so contracted, or stated to be the result of an accident while at work, has been the cause of numerous legal claims in France.

The book is the same size as the Bulletins of the Société française d'Ophtalmologie. The printing and paper are excellent; the author and the publisher are both to be congratulated.

Selected Studies in Visual Optics. By JOSEPH L. PASCAL. 1952. Pp. 769, 138 illus. Kimpton, London. (95*s.*)

Pascal's mode of writing, of tackling what appear to be difficult problems in optics and of rendering their solution apparently simple, are well known to readers of this Journal. He is an original thinker who has no objection to, in fact almost an affection for, unconventional methods and these are fully exemplified in the 46 chapters and appendix which go to the making of this book, a work based upon 40 years teaching experience. As stated in the preface, the author does not attempt to cover the whole field of visual and physiological optics, but has merely selected certain topics which he feels need clarification, and these he treats in a way which he hopes will stimulate thought and further research.

A good example of Pascal's method is afforded by his use of the metric unit of curvature of a lens. This unit is the reciprocal of the radius of curvature in metres and its employment in the Dam formula simplifies such problems as working out the optical power of the anterior or posterior surface of the cornea, of the crystalline lens in the eye, and of thick lenses generally.

Another useful conception is the accommodative unit, *i.e.* the amount of accommodation in dioptres necessary for focusing an object 1 metre from the eye. In corrected hypermetropes this is greater than unity and in corrected myopes less, a matter which is of some importance in the correction of presbyopia, especially in cases of anisometropia. The author's best-known work is probably that in connection with the use of the cross cylinder and his convincing demonstration of the necessity for keeping the astigmatism mixed during the test. This, needless to say, is gone into in considerable detail in the course of some 33 pages.

That the author has had much experience with students, is shown by the many mnemonics he quotes, and by his wisdom in reserving the treatment of geometrical optics until chapter 35, when it receives full consideration. He also discusses matters other than the purely optical, and touches for example on orthoptics and the Bates system. In the

latter connection, he states from personal experience that Bates was " not anywhere near as rabid about the efficiency of his methods or the degree of his success as some of his successors and followers are ".

The last two chapters deal with the extra-ocular muscles and the author's benzene ring schema for illustrating their actions. Though meant as a simplification, this seems to the reviewer to be much more difficult to follow than Duane's conception of primary and secondary actions and the two simple diagrams by which they can be worked out. The book concludes with an appendix containing a useful glossary of terms and symbols, and a full bibliography.

Summing up, this volume is one which literary critics, if they understood it, would describe as " important " ; it sheds welcome light on some of the dark corners of ophthalmology and as such will be appreciated by those who teach this subject.

Ophthalmic Pathology, an Atlas and Textbook. By J. S. FRIEDENWALD, H. C. WILDER, A. E. MAUMENEE, T. E. SANDERS, J. E. L. KEYES, M. J. HOGAN, W. C. OWENS and E. U. OWENS. 1952. Pp. 489, 240 plates. Saunders, Philadelphia and London. (90*s.*)

Most ophthalmologists are well acquainted with the "Atlas of Ophthalmic Pathology", which first appeared in 1938 under the editorship of DeCourcy and Ash and was based on the great mass of material which continually finds it way to the Registry of Ophthalmic Pathology of the Army Medical Museum in Washington. It was an unusually good publication and many students and practitioners of our specialty throughout the world learned much from the superb pathological illustrations it contained. The Registry of Ophthalmic Pathology in Washington—and it is interesting that the ophthalmic branch of the Registry is the oldest of its component parts—contains a wealth of pathological and histological material that is unmatched anywhere in the world. That this should go a-begging would be a tragedy, and it was indeed fortunate that the Armed Forces Institute of Pathology combined with the American Academy of Ophthalmology and Otolaryngology in commissioning a group of ophthalmologists to prepare a more ambitious project than the previous publication. In its new form the volume combines an atlas with a textbook of unusually high standard, the basis of which is Friedenwald's well-known book—" Pathology of the Eye " (now out of print)—which has been brought up to date for the purpose; it deals with the normal anatomy and physiology of the eye, its histology, its growth and senescence, and the general nature and mechanism of inflammation, and then continues in the rest of its 18 chapters to discuss systematically the whole of ocular pathology. The text is illustrated by a multitude of superb histological photographs. The result is a pathological treatise with which nothing in the ophthalmic literature of any country can be compared.

Reviewed in *Ophthalmic Literature*.

Contact Lenses, Clinical and other Observations. By J. M. ANDERSON. 1952. Pp. 40. Courtenay Press, Brighton. (7*s.* 6*d.*).

NOTES

MR. T. KEITH LYLE, F.R.C.S., Ophthalmic Surgeon to King's College Hospital, is to be a guest-lecturer at the jubilee celebrations of the Ophthalmological Society of Egypt, Cairo, in February, 1953.

Royal Eye Hospital Clinical Society

The February meeting will be held at the Royal Eye Hospital on Wednesday, February 25, 1953, at 6 p.m. Miss J. M. Dollar and Miss M. Savory will show their film "Exenteration of the Orbit", which will be followed by a discussion. Relevant cases will be demonstrated at 5.30 p.m.

The Order of St. John of Jerusalem

New Ophthalmic Foundations have been established in South Africa and in Jerusalem, Jordan. In each instance this is the only hospital in the country dealing with ophthalmic cases only. It is thus essential that a reference library be built up covering all aspects of ophthalmic work, and any gifts of journals or publications from organizations or private individuals will be very much appreciated. Gifts may be sent to the following addresses:

For Jordan:—The Order of St. John, St. Johns Gate, London, E.C.1.

For S. Africa:—The St. John Ophthalmic Foundation,
P.O. Box 7137, Johannesburg, Union of South Africa.

XVIII International Congress of Oto-Neuro-Ophthalmology, 1953

The Congress will be held in Bologna, Italy, from May 3–7, 1953, under the chairmanship of Professor Q. Di Marzio. The two main discussions will be on "Dysraphia in Oto-Neuro-Ophthalmology" and "Ménière's Disease".

Those wishing to attend or to submit papers should apply to the General Secretary, Dr. Giuseppe Cristini, Clinica Oculistica-Policlinico, Bologna, Italy.

Medical Research Council

Alexander Pigott Wernher Memorial Travelling Fellowships in Ophthalmology and Otology 1953-54

The Medical Research Council invite applications for Travelling Fellowships in Ophthalmology and Otology for the academic year 1953-54, for which special provision has been made by the Alexander Pigott Wernher Memorial Trustees. Under the terms of the bequest, the funds are to be applied "towards the prevention and cure of blindness and deafness in the United Kingdom and British Empire and in particular research in connection therewith by financing medical men and students within the Empire to study methods and practices in all countries of the world."

These fellowships are intended for suitably qualified medical graduates who are likely to profit by a period of work in ophthalmology or otology at a centre abroad before taking up positions for higher teaching and research in these branches of medical science. Candidates will be required to submit an outline of their proposals for work at a selected centre. The awards will normally be tenable for one year; no provision can be made for travelling grants for short-term visits abroad.

The fellowships provide for the payment of a maintenance allowance at the rate of £650 per annum for a single Fellow, or £900 per annum for a married Fellow, subject

to appropriate adjustment in the case of fellowships tenable at centres outside the sterling area. An allowance is made for travelling and other approved expenses.

Forms of application may be obtained from the Secretary, Medical Research Council, 38, Old Queen Street, London, S.W.1, with whom applications must be lodged by March 31, 1953.

HONOURS

NORMAN MCALISTER GREGG, M.C., CH.M. Sydney, F.R.A.C.S., Ophthalmic Surgeon to the Royal Prince Alfred Hospital, Sydney, Australia, has been created a Knight Bachelor.

OBITUARY

ROBERT MILNE DICKSON

ROBERT MILNE DICKSON, O.B.E., M.D., D.O.M.S., who died suddenly on November 8, 1952, in his 71st year, had been Director of the Ross Foundation for the Study of the Prevention of Blindness for 15 years.

Born on December 13, 1880, Dickson graduated in Medicine at St. Andrews University in 1906 and joined the R.A.M.C. in 1908. After a period as M.O. to the Royal Scots, he went to India early in 1910 and served with the 8th Hussars. At the beginning of the first world war he transferred to the King's Dragoon Guards and went with them to France in October, 1914. He was mentioned in dispatches for attending the wounded under fire, and was himself severely wounded at Hooge in May, 1915. While convalescing he wrote his M.D. thesis on spinal paralysis, a condition of which he had thus gained first-hand experience.

During a second period in India he had unusually extensive ophthalmic operative experience, and when he returned to England in 1927 he was appointed Eye Specialist at the Queen Alexandra Hospital, Millbank, London. In 1933 he became senior M.O. in Ceylon where he re-organized the medical service in the Ceylon Defence Force; in 1936 he was gazetted Colonel and returning to England was appointed A.D.M.S., Home Counties Area.

The following year he was made Director of the recently formed W. H. Ross Foundation for the Study of the Prevention of Blindness, Edinburgh (later extended to Scotland), and he remained in this post until his death, except for a period from 1939–41 when he served as A.D.M.S., Edinburgh Area, and went to Orkney and elsewhere to organize medical services.

Dickson was a keen sportsman and an excellent rifle shot, and one of the heads shot by him in India appears in Roland Ward's Book of Records. In later life he became an enthusiastic fisherman, and he caught his last salmon only two months before his death. While he was director of the Ross Foundation he interested himself in the research work which led to the discovery of sodium sulphacetamide as a remedy for external eye injuries, especially for hypopyon ulcer, and he organized its use in first-aid treatment in mines and factories. He also undertook a Statistical Analysis of Persons Certified Blind over the North and East of Scotland, and, with Dr. John Marshall and Dr. Seiler, presented an important comprehensive Statistical Statement for the whole of Scotland.

It was most fortunate for the work of the Ross Foundation that a man of Colonel R. M. Dickson's training and knowledge, devotion and personality was chosen as whole-time ophthalmologist. His work was greatly appreciated and his loss is deeply deplored.